Publication Number 36

AMERICAN LECTURE SERIES

A Monograph in

AMERICAN LECTURES IN ENDOCRINOLOGY

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Obesity...

By

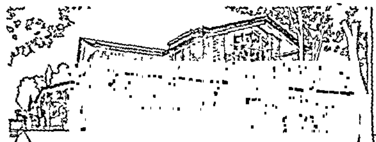
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CHARLES C THOMAS • PUBLISHER

Springfield • Illinois • U.S.A.

CHARLES C THOMAS • PUBLISHER
BANNERSTONE HOUSE
301-327 EAST LAWRENCE AVENUE, SPRINGFIELD, ILLINOIS

Published simultaneously in The British Commonwealth of Nations by
BLACKWELL SCIENTIFIC PUBLICATIONS, LTD., OXFORD, ENGLAND

Published simultaneously in Canada by
THE RYERSON PRESS, TORONTO

First Edition

FOREWORD

THIS monograph has been prepared for the use of the practicing physician rather than for the investigator in this field Therefore, the bibliography includes only those articles which may be obtained and read relatively easily References to articles in foreign languages have been kept at a minimum. More detailed and comprehensive information can be obtained by referring to the splendid articles by Newburgh, Bruch, Evans, and Rony in particular. Much of the important German literature has been reviewed by Wilder. We are indebted to Alice Karslake Irmisch for the preparation of the chapter on diets.

E. H R.
C F G

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Obesity...

Chapter I

INTRODUCTION

THE WORD obesity is derived from the Latin "obesus which means "eaten up" or "lean," gradually the term came to have the opposite meaning, that of being overweight[365] The term "adiposity" may be used as a synonym and is perhaps a better choice since it is derived from the Latin "adeps" meaning "fat"[158]

To define obesity is difficult and most of the definitions given have been quite arbitrary[82] Sevringhaus[339] defined obesity as an excess of fat over the normal expected for the height, age and sex of the patient Bruch[63] defined obesity as a nutritional state in which the storage of fat exceeds the amount that is commonly associated with an expression of adequate alimentation Newburgh[289] defined the condition as a state in which the body contains an abnormally large amount of adipose tissue Epstein[122] held that obesity signifies an increase in body weight in excess of the limitation of skeletal and physiologic requirement, owing to the deposition of fat.

Still another definition, given by Bauer,[17] states that the term "obesity" should be limited to those persons who, if left to their own automatic regulation of diet and activity, exhibit a compulsory tendency toward a pronounced and abnormal accumulation of fat He would not apply the term "obesity" to the condition resulting from simple overeating, but rather to that inherent constitutional abnormality which leads to obesity. In fact, he expressed the opinion that stoutness could not arise from increased appetite due to faulty habits of eating. Such distinctions seem unnecessary, however.

Life insurance statistics [263] show that the average weight, as given in the usual height-weight tables, after thirty years of age is too high and that for optimal life expectancy one should not weigh more than the average at thirty years. Wilder [407] concurred in this view. It is felt that longevity is probably the best single index to the ideal weight [263, 264] and if this premise is accepted, the tables of "ideal weight" are found to be considerably different from the ordinarily used tables of average weights The weight of the average person increases about twelve pounds (5 kg.) between the ages of twenty-five and fifty years, but this is true because many are gaining twenty or thirty pounds (9.1 to 13.6 kg.) or more and some are remaining constant in weight. It has been shown that maximal life expectancy is obtained if the average weight at ages twenty-five to thirty years is maintained the remaining years of one's life.[263, 264] For this reason it is suggested that Tables I and II be used to determine the ideal weight of adult patients. These first two tables also have the advantage of allowing for variations in body build. Statistical studies by life insurance companies have also demonstrated that it is of some advantage to be slightly over average weight before the age of thirty years, to be of average weight from ages thirty to forty and to be definitely underweight after age forty.[262]

In allowing for variations in body build, some authors allow a 10 per cent range on either side of normal.[339] A more exact method, which considers the variations in bodily proportion, is the determination of specific gravity.[23] The lower the specific gravity, the greater the amount of adipose tissue in relation to other structures. Because this method requires weighing the patient under water, it will not likely become a common one. A close correlation has been found between thoracic and abdominal measurements, and such measurements have been considered to be an adequate substitute for the elaborate procedure of underwater weighing.[22]

It has been stated that obesity is the most frequent physi-

TABLE I

IDEAL WEIGHTS FOR MEN OF AGES 25 AND OVER *
Weight in pounds according to frame
(as ordinarily dressed)

Height (with shoes on) Feet	Inches	Small Frame	Medium Frame	Large Frame
5	2	116–125	124–133	131–142
5	3	119–128	127–136	133–144
5	4	122–132	130–140	137–149
5	5	126–136	134–144	141–153
5	6	129–139	137–147	145–157
5	7	133–143	141–151	149–162
5	8	136–147	145–156	153–166
5	9	140–151	149–160	157–170
5	10	144–155	153–164	161–175
5	11	148–159	157–168	165–180
6	0	152–164	161–173	169–185
6	1	157–169	166–178	174–190
6	2	163–175	171–184	179–196
6	3	168–180	176–189	184–202

* From Metropolitan Life Insurance Company [84]

cal abnormality found in the general population.[115] Approximately 28 per cent of the population are 10 per cent or more overweight (Table III). The gain in weight with advancing age is greater in women than in men, and a greater proportion of women are overweight than men (Fig 1).[115] In childhood the incidence of obesity is about equal in the two sexes.[68]

The handicaps imposed by obesity have been enumerated by many authors but frequently the physician fails to emphasize sufficiently to the patient the seriousness of this disease. It is easy to shrug off "a few pounds of overweight"

TABLE II

IDEAL WEIGHTS FOR WOMEN OF AGES 25 AND OVER *

Weight in pounds according to frame
(as ordinarily dressed)

Height (with shoes on) Feet	Inches	Small Frame	Medium Frame	Large Frame
4	11	104–111	110–118	117–127
5	0	105–113	112–120	119–129
5	1	107–115	114–122	121–131
5	2	110–118	117–125	124–135
5	3	113–121	120–128	127–138
5	4	116–125	124–132	131–142
5	5	119–128	127–135	133–145
5	6	123–132	130–140	138–150
5	7	126–136	134–144	142–154
5	8	129–139	137–147	145–158
5	9	133–143	141–151	149–162
5	10	136–147	145–155	152–166
5	11	139–150	148–158	155–169

* From Metropolitan Life Insurance Company[262]

as something of little consequence, but in so doing, the physician is ignoring what is perhaps his best chance to lengthen the life and diminish the future illnesses of his patient (Tables IV and V and Fig 2). Statisticians have recently pointed out the increase in deaths from the degenerative diseases, such as heart disease, diabetes and cancer;[405] the implication has been that medicine is approaching a point of diminishing returns and that increasing efforts will reduce the death and illness rates only slightly. Actually a great improvement in the health of the nation is possible by means of the correction and prevention of obesity. In time of war, countries with diminished supplies of food have

TABLE III

PERCENTAGE INCIDENCE OF OVERWEIGHT AND UNDERWEIGHT AMONG 10,000 EXAMINERS *

		Actual	Standardized†
Overweight 10% or more	Men	25 8	25 7
	Women	30 9	30 3
	Total	27 3	28 0
Underweight 10% or more	Men	10 2	10 2
	Women	15 8	15 3
	Total	11 9	12 8

* From Editorial[114]

† Standardized for age and sex according to the population of the United States in 1930

demonstrated a definite decrease in the incidence of degenerative diseases.[264]

Statistical studies demonstrating the adverse influence of obesity on hypertension,[172, 227, 228, 346, 351, 382, 418] pulmonary emphysema,[209, 350] diabetes,[132, 172, 196, 276, 283, 286] heart disease,[227, 254, 345] cancer,[303, 380] acute and chronic nephritis,[104, 106, 227, 366] cirrhosis,[104, 205, 366] appendicitis,[104] accidents,[104] venous thrombosis and embolism,[15] atherosclerosis[412] and toxemias of pregnancy,[258, 294] all suggest that by the treatment of obesity the physician may ameliorate considerably the effects of many diseases for which otherwise he has little really effective treatment. The increased dangers of surgical procedures in the presence of obesity,[19, 82, 105, 112, 129] the greater severity of degenerative arthritis in the knees, hips and lumbar spine of the obese,[63, 78, 91, 129, 274] increased incidence of gallbladder disease,[34, 105, 129] earlier appearance of varicose veins,[91, 106] more frequent fractures,[82] increased fetal mortality and greater difficulty in obstetrical delivery[258] are further reasons for the correction of obesity. It is probable that a longer duration of the obesity increases the chances of development of both hypertension and diabetes.[77, 166, 293, 346] It has been suggested that since one

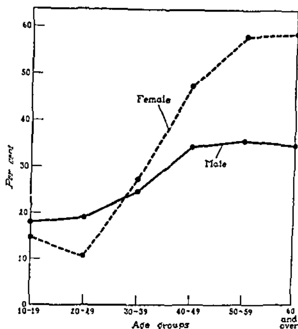


Figure 1. Incidence of overweight (10 per cent or more) among 10,000 examinees for insurance by age and sex (From Editorial: A study of impairments found among 10,000 unselected examinees. Article II; Weight. *Proc. Life Ext. Exam* 1.89-93 [July-Aug] 1939.)

action of insulin is to convert carbohydrates to fat,[103] a process of considerable magnitude in the development of obesity, the demand for insulin is correspondingly great and may exceed the capacity of the pancreas to produce it; thus, diabetes may result

Smith and Willius[360, 415] in their study of the pathology of adiposity of the heart found that the degree of cardiac enlargement in obesity is roughly proportional to the increase in surface area and that some of these otherwise normal, enlarged hearts may fail They consider "adiposity of the heart," which frequently accompanies obesity, as an increase in the amount of subepicardial fat and of the fat lying be-

TABLE IV

DEATHS PER 100,000 — ALL CAUSES — ALL AGES COMBINED BY WEIGHT CLASSES *

	Death rates per 100,000	Percentage of rate in "normal" weight class
Underweights		
15% to 34% underweight	913	108
5% to 14% underweight	833	99
Normal weights	844	100
Overweights		
5% to 14% overweight	1,027	122
15% to 24% overweight	1,215	144
25% or more overweight	1,472	174

* From Editorial [313]

TABLE V

INFLUENCE OF OVERWEIGHT ON MORTALITY IN PERSONS AGED 45 TO 50 YEARS *

Pounds overweight	Increase in death rate over average, per cent
10	8
20	18
30	28
40	45
50	56
60	67
70	81
90	116

* From Newburgh, L. H [304]

tween muscle bundles; fatty infiltration, on the other hand, is seen in pernicious anemia, carcinoma and similar conditions and consists of droplets of fat which appear within the cytoplasm of the cardiac muscle cells

Obesity causes a diminished vital capacity probabl through the mechanical restriction of respiratory movement by deposits of fat in the abdominal and thoracic walls. I the duration of the obesity is great enough, emphysema de velops and the vital capacity is permanently impaired in spit of later adequate reduction in weight.[209, 350] Evidence ha been presented that a considerable degree of exertiona dyspnea can occur without a significant degree of impair ment of cardiac output, the dyspnea presumably resultin from the decrease in vital capacity alone.[306] Obese person have been found to be less able than the nonobese to toler ate exertion at high temperatures and humidity.[322] Electrocardiographic changes in obesity are frequently seen.[254, 345] Diaphragmatic hernia is more frequently observed in the obese and it occasionally may be corrected by weight reduction alone.[34] Further, surgeons have found that the ease and success of a repair of a diaphragmatic hernia is greatly increased by the correction of obesity.

In addition to the physical disorders mentioned, there are serious psychologic problems stemming from obesity. Marked obesity is essentially a repulsive disease; its victim tends to feel rejected, unable to join with others in many of the ordinary activities with complete acceptance. Because physical activity requires greater effort for the obese than for the nonobese, the victim is likely to retreat to a state of inactivity and thereby to perpetuate and accentuate the condition The frequent occurrence of neuroses in the obese has been emphasized by several investigators.[63, 69, 70, 291, 316] It should be pointed out, however, that similar psychologic investigations of control groups of nonobese persons might have revealed a similar incidence and variety of neuroses. It is, of course, difficult to judge what proportion of psychologic difficulties is the result of, and how much is the cause of, the obesity.[1]

Esthetic reasons for the treatment of obesity are not the least important. The desire to be attractive is possibly the

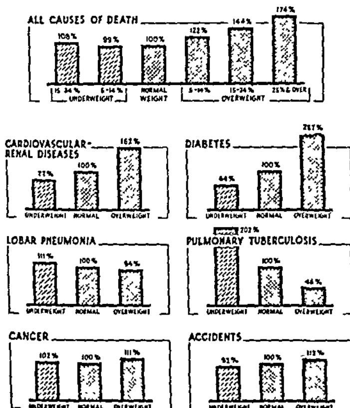


Figure 2 Influence of body weight on mortality from selected causes (From Dublin, L. I.)

most frequent reason that the overweight person goes to the physician for help in reduction, although in some cultures obesity has been considered a mark of beauty.

While there is no question but that obesity increases the incidence of a large number of pathologic processes, it cannot be assumed with such certainty that the reduction of the weight of an obese person to normal will give him health equivalent to that of the person who has never been obese. Some of the changes caused by obesity, such as emphysema,[209, 350] tend to become irreversible in time, but others may be corrected by reduction of weight.[228] It seems reasonable to assume that the shorter the duration and the less the degree of the obesity, the more easily will normal health expectancy be restored. It is, therefore, as important to prevent as to correct obesity.

In consideration of all these factors, it would seem desirable that more doctors develop something of the missionary spirit and zeal in correcting obesity.

Chapter II

PHYSIOLOGY OF OBESITY

BEFORE the controversial questions of treatment and etiology are considered, it is best to have some understanding of the physiologic mechanisms involved in obesity.

Early in the investigations of obesity, several cases were reported in which there appeared to be a maintenance of obesity in spite of low caloric intakes.[121, 268, 373, 387] These findings seemed to confirm the popular idea that there are fat people who stay fat no matter how little they eat[118, 372] However, in more recent and better controlled studies it has been shown that obese persons must eat more than the average person in order to remain obese.[81, 268, 282, 285, 370] This statement has been made previously in many forms and for emphasis it is here repeated: *Fat comes only from food, and* [illegible]

those with a tendency toward leanness who can overeat with impunity and that there are those with a predisposition to obesity who will become fat although they eat no greater amount than does the lean person[136, 372] It is apparently felt by these investigators that some obese persons have an unusual mechanism, not possessed by other people, for conserving energy It is sufficient to say that such a mechanism has never been adequately demonstrated[384, 385] and that the very multiplicity of suggested abnormalities of metabolism argues against such a possibility

The wonderfully integrated ability of the body to maintain itself in a constant state has been the subject of many discussions The French physiologist, Claude Bernard, was

the first to make an extensive study in this field He coined the term "milieu interieur" and emphasized the remarkable stability of the composition of body fluids. Cannon[70] developed this concept further under the designation "homeostasis." Von Noorden[387] and Levy expressed the belief that the ingestion of only a small excess of food daily would soon result in obesity. This idea that a small continuing strain would ultimately cause a larger error in metabolism disagrees with the concepts of *Bernard and Cannon* as developed by Gamble.[140] Gamble emphasized the ability of the bodily compensatory mechanisms to minimize and obscure the effects of any of the lesser strains on the various metabolic processes. Nevertheless, the ingestion of food appreciably in excess of requirements is a stress with which the body has only limited ability to cope, and a gain in weight of some degree will invariably follow. Therefore, the mechanism which determines appetite is a primary factor in the development of obesity.

No one has been able to explain satisfactorily what determines satiation, but it probably depends on the interaction of a number of factors.[74] The striking effect of hypothalamic damage in producing obesity *through increased* appetite[45] suggests that an important center for normal appetite regulation may reside there. The importance of psychic conflict in the development of obesity in persons exhibiting compulsive eating has frequently been observed,[84] thus demonstrating that the cerebral cortex may override the more automatic and primitive appetite control centers.

It is the familiar plaint of the fat person that "I don't eat a thing and I still get fat" It has been well proved that *they do eat excessively,*[282, 370] *and it is interesting to speculate* why this belief should arise so frequently. A possible explanation is that the person with a predisposition to obesity has an appetite mechanism (whatever that may consist of) which requires a larger than normal amount of food before satiation is accomplished If he eats what would satisfy the

normal person he remains hungry and feels that he has eaten very little; if he eats anything less than what is required for satiation he is likely to believe honestly that he has eaten little, even though he has consumed large quantities of food A corresponding situation appears to exist for the person with a tendency toward leanness who insists that he eats a great deal and still fails to gain

Hunger has been defined as an unpleasant sensation, physiologic in origin, best described as a hollow, empty feeling in the epigastrium, while appetite is considered to be a desire for the pleasurable sensations associated with food and drink and is of psychologic origin.[76, 79] Both of these sensations lead to eating, however, and for our purposes they may be considered identical. The two terms will be used interchangeably.

It was suggested by Cannon[76] that hunger was associated with gastric contractions, and it has been shown that insulin-induced hypoglycemia will increase the concentration and amount of gastric acids by means of vagal stimulation[183] From this it would be easy to assume that lack of food leads to hypoglycemia; hypoglycemia causes increased gastric activity by means of vagal stimulation, and the increased gastric activity is in turn responsible for the sensation of hunger. It has been demonstrated, however, that denervation of the stomach does not prevent insulin-induced hunger in dogs[182] Thus, there must be other alternate mechanisms

The efficacy of the odor and sight of food, and even of mere memories of good meals, in arousing appetite is familiar to everyone Other theories of hunger and appetite involve cerebral "hunger centers" and peripheral nerve impulses from chemosensitive tissues which detect changes in the composition of blood, such as the change in hypoglycemia.[79]

It is more likely that hunger depends on the summation and integration of a large number of sensory impulses and that the complex mechanism by which it is aroused varies in

its function from person to person, and even from time to time in the same person. Maclagen[246] performed fundamental animal experimentation which showed the effects of fasting and of various drugs on appetite. The optimal duration of a fast for stimulating appetite was found to be eighteen hours.

In addition to variations in food intake as a means of regulating weight, there are also other mechanisms which involve changes in the output of energy.[290, 323] More specifically, Newburgh has shown that the person fed a diet slightly greater than that which he required for maintaining his weight does not continue to gain indefinitely, but rather gains weight quickly at first, then more and more slowly as he approaches the increased weight at which the increased diet will maintain him. This mechanism for limiting the gain in weight seems related in some manner to the surface area

It has been well demonstrated that the number of calories required by the body at resting state is proportional to the surface area [260, 301, 369] Thus a 35 year old man, 5 feet and 7 inches (170 cm.) tall with a surface area of 1.79 square meters, will maintain a normal weight of 150 pounds (68 kg.) *with an intake of 2,415 calories each 24 hours* (Table VI) If he consumes 3,255 calories (34 per cent more) he will gradually gain in weight until he reaches 300 pounds (136 kg.) and a surface area of 2 4 square meters (34 per cent greater). The weight gain by such a man weighing 150 pounds and eating 3,255 calories will at first be 1.7 pounds (0.8 kg) per week The rate of gain will gradually become slower until gaining ceases at 300 pounds Similarly if this man weighed 300 pounds and were fed 2,415 calories daily he would lose 1.7 pounds a week at first, the rate of loss gradually slowing as his weight approached 150 pounds From these figures * it can be seen that a small daily excess of food does not lead to unlimited gains in weight as was

* Calculations were made by means of the Boothby-Berkson nomogram and the factor for predicting loss of weight given by Wilder.[illegible]

once postulated by Von Noorden,[387] but rather to definite calculable and limited increases This removes some of the mystery with which the appetite mechanism was surrounded when Von Noorden pictured it as a device of almost incredible accuracy. It also diminishes the necessity for postulating obscure aberrations in the metabolism of energy which would adjust the output of energy to fit the intake

TABLE VI

VARYING FOOD REQUIREMENTS FOR A THIRTY-FIVE YEAR OLD MAN AT DIFFERENT BODY WEIGHTS *

Weight, pounds	Surface area, square meters	Calories required per twenty-four hours	
		At basal conditions	With moderate activity†
100	1 50	1,360	2,040
150	1 79	1,610	2,415
200	2 02	1,840	2,760
250	2 22	2,020	3,030
300	2 40	2,170	3,255

* These calculations assume a basal metabolic rate of 0 and were obtained by use of the Boothby Berkson nomogram for a thirty-five year old man 5 feet and 7 inches tall who had a standard weight of 150 pounds. (From Gastineau, C. F and Rynearson, E H Obesity *Ann Int. Med*, 27 883 897 (Dec) 1947.)

† Caloric requirements at moderate activity are assumed to be 50 per cent greater than those at basal conditions

The relation of surface area to the rate of metabolism, which was first noted by Rubner,[103] is the basis for basal metabolic standards [260, 301, 369] The fact that basal metabolic rates are found to be normal in obesity has great importance.[87, 61, 107, 194, 259, 260, 304, 373, 374, 379] It means that the obese person has a much greater rate of metabolism than he would have if he were of normal weight. He is eating more to maintain a metabolic fire of greater size His circulatory and respiratory systems are carrying loads greater than

they were designed to carry. It is as though a passenger car motor were being used to propel a truck. Because standards are computed on the basis of surface area, this increased rate of metabolism is obscured by the normal basal metabolic rates found in obesity. The increased rate of metabolism in obesity has been compared to that seen in hyperthyroidism; indeed, there are certain clinical similarities in the tachycardia, cardiac failure, easy perspiration and other symptoms [369]

It has been suggested that the excess adipose tissue in the obese is inert and that all of the exchanges of energy are taking place in the muscles and viscera.[349, 369] Talbot,[379] however, expressed the belief that the adipose tissue in children contributes an appreciable fraction of the bodily heat production McCune and Bruch considered it virtually impossible to estimate "active mass" in obese children [241] Mirski [266] characterized adipose tissue not as a passive source of stored fat but as an active organ with a specific carbohydrate metabolism, a concept supported by the experimental studies of Schoenheimer [332]

Reduction of the caloric intake of an obese person may lower the basal metabolic rate, according to some authors,[58, 83, 88, 261, 369] but others have failed to find such a decrease.[127, 268, 275, 323] These contradictory reports may be explained by the fact that in the various studies different diets were utilized. Although all diets were inadequate in calories, some contained much larger amounts of protein than others. It is possible that a generous supply of protein may prevent this fall in the basal metabolic rate, although the basal metabolic rate is properly determined after an overnight fast when any effect of specific dynamic action should be absent. This question of the fall of the basal metabolic rate in the reduction of weight of obese persons is of some importance, but insufficient studies have been made to permit the formation of any definite conclusion. In spite of whatever lowering of the basal metabolic rate may occur, it seems fairly certain

that the rate of energy exchange never quite falls to that of the patient at normal weight Expressed in other terms, the basal metabolic rate computed on the basis of ideal weight will be perhaps a + 25 in an obese subject A lowered caloric intake may reduce somewhat this elevated basal metabolic rate before there is more than a moderate loss of weight, but the rate does not reach the zero level until the patient's weight reaches normal [369] The starvation of the normal or thin subject is an entirely different matter [232, 255, 323, 369] In such subjects the heat production diminishes markedly, work becomes difficult and there is much depression and emotional instability,[210] greatly in contrast with the increased feeling of well-being observed by obese patients who are undergoing successful reduction of weight [369] Some of the lowest basal metabolic rates are seen in anorexia nervosa, one of the clinical forms of starvation In contrast the obese patient during reduction has increased vigor, remains active and feels quite well

The mechanisms which regulate metabolism thus tend to cause weight to remain within certain limits with certain variations of food intake. An increase in caloric intake causes weight to rise to a new level and then to be maintained, a decrease in diet causes the weight to descend to a new level where it will remain constant on a given supply of energy.

Another result of obesity is a diminution in the tolerance for carbohydrates [286] This phenomenon is observed more frequently in patients with long-standing obesity than in those with obesity of short duration [77, 186, 283, 295] but it is not an invariable companion of obesity.[21] If the patient is over forty years of age at the onset of glycosuria it is likely that reduction of weight will remove all evidence of disordered metabolism of carbohydrate Newburgh [286] expressed the belief that this variety of glycosuria and hyperglycemia is distinct from true diabetes It would be difficult and of no great importance to prove that the hyperglycemia

is not the manifestation of a latent diabetes which is brought into the open by the obesity.

There is little difference between the obesity of childhood and that beginning in adult life. Obese children, judged by all criteria of development, are usually somewhat advanced[60, 66] except in social and emotional aspects. The basal metabolic rate is essentially normal although standards are very uncertain[61, 879] There are particular difficulties in estimating the progress and degree of obesity in children because of the constantly changing mass of skeletal and muscular tissue[67] but various devices, such as the grid devised by Wetzel, may aid in overcoming this difficulty.[67, 402] Reduction of weight may possibly lead to an earlier puberty[66, 878] although obese children characteristically are advanced in this respect.

Amenorrhea, sterility, and even dysmenorrhea have been ascribed to obesity.[11, 127] Certainly, amenorrhea and sterility in the presence of obesity cannot be said to be good evidence for an endocrine etiology for obesity and are most likely secondary to obesity

In summary, it can be said that the various phenomena observed in obesity are chiefly the result of it and not evidences of some quirk of metabolic processes which have caused the disease. Numerous errors of metabolism have been suggested as the cause of obesity and these will be discussed in the next section.

Chapter III

ETIOLOGY

NUMEROUS classifications of obesity have been made[14, 118, 323] and it is significant how little agreement there is among them The concept of endogenous and exogenous obesity was championed early in the century by Von Noorden[387] and it has remained popular since[111, 334] Engelbach[121] stated that endogenous obesity does not respond to dieting and exercise while the exogenous variety does Newburgh makes no distinction between exogenous and endogenous obesity, stating that obesity is always caused by the consumption of food in excess of requirements, a conception of obesity which many would label exogenous His well-controlled studies invariably have demonstrated that the obese person loses weight on a submaintenance diet in accord with metabolic calculations On the other hand, it has been argued that all or most obesity is endogenous since the factors which initiate the overeating, such as psychologic conflicts or hypothalamic damage, originate within the person.[173, 184, 208, 354] It would seem wisest to abandon the terms "endogenous" and "exogenous" obesity[329]

Bernhardt[28] presented an involved classification Goldzieher[148, 149] maintained that there are many causes of obesity and that it should be regarded as a symptom common to many conditions rather than as an entity For this reason and others he criticized Newburgh and other workers who have advanced our knowledge of obesity tremendously by the detailed study of individual patients

The etiology of obesity will be discussed under a number of headings in this paper but the outline should not be taken as a classification of obesity. Rather the outline should be

considered as a list of mechanisms which have been proposed, of which only a few have been accepted as of any importance

THE HYPOTHALAMUS

Injury to the hypothalamus has been shown to interfere with such important self-regulatory functions as temperature control, water balance, appetite, gastro-intestinal function and sleep [56, 144, 311] Damage to certain portions of the hypothalamus causes poikilothermia, that is, the animal loses the ability to control its temperature by means of sweating and vasomotor mechanisms and assumes the temperature of its surroundings Damage to the paraventricular hypothalamic nuclei will cause obesity to occur [171, 175, 176, 177, 403] as a result *of voracious, ravenous appetite* [45, 46, 57, 203] *which begins* abruptly after the injury. Diminished production of heat and reduced activity may play some lesser role in the development of obesity from this cause Altered habits of eating may also be a factor,[49, 50, 54] the rapid, single, large feedings of the animal with hypothalamic damage supposedly producing less of a specific dynamic action than the slower, smaller and more frequent feedings of the normal animals.[45] Heinbecker, White and Rolf [171] have shown that bilateral *destruction of the paired paraventricular nuclei is the crucial* factor in the production of this variety of obesity. They have contrasted this experimental finding with the effects of the destruction of the supra-optic nuclei in causing diabetes insipidus. These experimental facts explain a few rare types of obesity and, in addition, suggest that the hypothalamus may be the center which is normally in control of a great number of mechanisms which regulate a variety of bodily functions, among them being those of appetite and other aspects of energy exchange [47, 51] Bernhardt [28] was one of the first to suggest that the hypothalamus may play an important role in the development of common obesity.

In 1840, Mohr reported the case of a woman in whom

obesity developed rapidly before the patient died of a large pituitary tumor. In 1901 Frohlich described a patient who exhibited hypogenitalism, obesity, infantilism and a tumor at the base of the brain.[20, 62] It was at first assumed that these changes resulted from the destruction of the pituitary body and Cushing[87] seemed to confirm this opinion Erdheim in 1904, however, maintained that damage to the base of the brain is primarily responsible for the adiposity which sometimes accompanies pituitary tumors. In 1912 Aschner[10] observed that only those animals with injury to the hypothalamus became obese after hypophysectomy. As evidence has accumulated it has become more and more apparent that at least the obesity in Frohlich's original case must have been the result of damage to the hypothalamic region.

The term "Fröhlich's syndrome" has been used frequently to describe the child or adolescent whose genitalia are partly obscured by masses of adipose tissue Such children may attain a more normal appearance spontaneously[48, 154] but many endocrinologists treat them with a variety of hormones[383] Bruch has warned of the real dangers of endocrine therapy in obese children She stated that the important factor of diet will be obscured by glandular therapy and that significant psychologic damage will be done to the child who is being treated for "gland trouble"[65] Some authors have described a syndrome similar to that of Fröhlich which is not associated with tumor and is thought to respond to treatment with pituitary extracts or to disappear spontaneously. Mittelmann described this under the term "juvenile adiposogenital dystrophy"[267] but it is doubtful whether this is an entity In view of the frequent misuse of the term "Frohlich's syndrome" to include patients without intracranial lesions and because of the doubtful nature of the condition known as adiposogenital dystrophy it would seem wise to abandon both these terms

The hypoplasia of the genitalia sometimes found associated with hypothalamic injury and obesity was at first

has suggested that emotional experiences can actually cause derangements of hypothalamic function thereby possibly causing the obesity that accompanies neurosis.

PSYCHOLOGIC FACTORS

As the phylogenetic scale is ascended, the cerebral cortex exerts an ever greater modifying influence on the functions of the lower nervous centers. In the maturation of the individual, the cortex also assumes a greater control over such basic functions as *eating, sleeping and procreation. There can* be no argument but that our civilization has modified all such functions tremendously, and the aspect that each presents in various cultures is chiefly a mirror of that culture. Rousseau's "noble savage," that hypothetical person reared free of all such cultural pressures and taboos, does not exist

Eating has acquired *a considerable social significance in our own social order, not only in the nature and time* of the meals but in the amount eaten.[180]

While it is true that most infants and children have less modification of their hypothalamic impulses by the cerebral cortex than do adults, yet Bruch[60] has shown in a series of fundamental articles that obesity of psychologic origin can begin early in childhood. The psychologic pattern of the mothers of these obese children is usually as distincitve as that of the children themselves. Such mothers usually go to extremes in protecting their children from even the minor conflicts of living but paradoxically entertain great ambitions for them. These children are prevented from striving with *other children and are bathed and dressed by their mothers* far beyond the usual age for such care. Often, the obese child, Bruch found, is the only or the youngest child in the family. Within the families containing obese children there is frequently great emphasis on food. Desserts and candies are used as rewards for good behavior; conversation centers around delicacies of the table, and the child gains the feeling *that food is* the end and purpose of life.[178] The mothers of

obese children were found by Bruch to be emotionally starved themselves, disappointed in their husbands, worried over domestic strife and often disappointed in the sex of their children. As if in compensation, these mothers attempt to pour out to their children a love that they do not honestly feel. In such an attempt they give the most obvious things, namely, food and protection from the unpleasantness of work and contact with other children "who might play rough," but these mothers are still unable to give their children true affection Such circumstances occur in the lives of many lean persons, however.

Such a situation acting on a child can lead to obesity in a number of ways. The protection from rough play and exertion diminishes the amount of energy expended[64] The atmosphere of gourmandizing and the continued urging to eat will cause the ingestion of increased amounts of food Furthermore, the emotional starvation of the child who perceives the real emptiness of his mother's show of affection may lead to a compensatory increase in food consumption as though the child were trying to satisfy his emotional hunger by the eating of food

While these factors have been repeatedly demonstrated by several observers, it may properly be asked whether similar factors do not frequently occur without the development of obesity This view finds some confirmation in the investigations of the etiology of anorexia nervosa.[310, 339] Here is a syndrome which is almost invariably a manifestation of an emotional conflict and which has many close similarities to obesity but which superficially is completely different. Both are disorders of the mechanism which regulates the quantity of food intake Frequently anorexia nervosa is preceded by obesity, or the two conditions may alternate.[339] Both are more frequent in women and both respond most dramatically when treated by means of proper diet and psychotherapy This response to diet and psychologic treatment alone is impressive when contrasted with the numerous articles which

urge the use of endocrine substances and which give support to endocrinologic theories of causation.

Johnson[191] reported the cases of a man who lost, and of his wife who gained, weight in response to the same emotional stress.

One of the most nearly universal drives is the one to save face, to put on a good front for other people to see.[291] In keeping with this desire is the great dislike of obese persons to admit that their disease is due to gluttony and their insistence that the doctor tell them that "it's your glands and we'll treat it with this gland extract"[291, 347] A program of endocrine therapy alone is greatly to the patient's immediate comfort, for it offers both preservation of self-respect and the illusory prospect of reduction by means of "gland extracts" while it permits continuance of the indulgence of appetite. *But unless the consumption of food is curtailed, no therapeutic program will succeed.* If the doctor once, even by implication, admits that "your trouble is glands" he may find it difficult to convince the subject of the importance of diet.[291] To tell the obese person that "there's nothing wrong with you except that you eat too much" might arouse immediate antagonism, but frequently such an approach is necessary.

It is striking how frequently the overweight person insists that he is a "small eater," and when given a properly balanced reduction diet of 1,000 or 1,200 calories he may insist that that is more than he ordinarily eats. There are several reasons for this. First, the obese person frequently eats many concentrated carbohydrates and, mistaking bulk for caloric content, underestimates the energy value of his customary diet. Second, the obese person hates to admit his gluttony and convinces his conscious self that he is actually in the habit of consuming relatively small amounts of food. Third, it is possible that the appetite mechanism is distorted in the person "predisposed" to obesity so that more food is required for his satiation than for the normal person. If he

eats a more than average amount but still not enough to satisfy his increased demand, the obese person will feel that he is eating only a small amount.[288] Similarly the thin person becomes easily satiated and, if he eats a normal diet, feels that he has eaten exceedingly heartily. Such psychologic and physiologic factors render the estimation of food intake by patients unreliable and misleading.

It is the physician's task to limit the caloric intake, to aid the patient to adjust to his emotional problems and to teach him new dietary habits so that he will not immediately relapse into overeating and obesity after completion of a successful reduction program. A better criterion for the success of a weight reduction program is the state of the patient's health two or five years after its initiation.

The emotional factors which led to obesity initially should not cause the physician to overlook the conflicts which result from the obesity and which tend to perpetuate it. The obesity itself becomes a handicap which prevents the patient from joining in play and from obtaining exercise, which in turn results in diminished output of energy and further gain in weight. The obesity is sometimes unconsciously used by the patient as a means of protection against doing unpleasant things. Obesity may repel suitors and may protect the obese girl from the responsibilities and duties of marriage.[320] It may play a part in the selection of an occupation, preventing the obese person from doing difficult work. The feeling of being "set apart" from other people because of the physical disfigurement tends to cause a certain amount of emotional starvation which perpetuates the increased appetite.

Occasionally the problems which precipitated the obesity may be solved by the changes in circumstance that time brings about, but usually some attempt to resolve the patient's difficulties must be made. Not only must the physician overcome the factors which initiated the gain in weight but he must also solve those which have arisen as a result of the obesity.

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Emotional depression frequently leads to loss of weight but it also may cause a definite increase.[316] In one well-studied series of fifty patients, Schopbach and Matthews[333] found mild anxiety states with considerable "neuromuscular tension" and obsessive-compulsive tendencies most common. In this group, eating frequently served as a device to diminish tension. In all but five or six patients of the series, psychogenic factors seemed closely related to the onset and development of obesity. This correlation of insecurity and obesity is emphasized in Bruch's studies which showed that families whose financial condition was on the borderline of inadequacy tended to have obese children. Thus the fear of not having enough to eat leads to overeating. It is also true, however, that the cheaper foods, which are chiefly concentrated carbohydrate, are those with a low satiation value.

Ingestion of alcohol possibly may stimulate appetite sufficiently to lead to obesity; in addition, alcohol itself has a definite caloric value[240] It is also well known that the ingestion of alcohol is associated with many psychologic factors.

A number of observers have suggested that "nervous shocks and strains" may cause obesity by modifying autonomic functions, but this proposal has never been confirmed.[180]

A freudian concept of obesity as a manifestation of orality has been presented[43, 145] and Richardson[320] has suggested that the ingestion of food may be given the symbolic meaning of impregnation. Bram[43] has also noted that other fat people will frequently discourage the patient from following his diet. Hill[178] associated gastro-intestinal symptoms, including emaciation and obesity, in adult life with patterns of breast feeding.

ENDOCRINE FACTORS

One of the most regrettable practices in medicine is the attempt to diagnose numerous endocrinologic aberrations

by means of slight variations in distribution of body fat.[121, 148, 149, 188, 200] These elaborate classifications into types have little or no basis in controlled experiment and are usually misleading.[158, 159]

Pituitary

First advanced by Fröhlich, the concept of an obesity secondary to hypopituitarism has disappeared slowly[62] although, as stated before, there is little or no justification for its existence. Traditionally the patient with so-called pituitary obesity has a large trunk and slender wrists and ankles,[121] if this condition is associated with dwarfism, it is known as the "Burnier" type of obesity.[113] Although hypophyseal obesity is ascribed by many to disorders of the anterior lobe, Werner[400] placed the blame on a lack of posterior lobe secretions and used pituitrin as substitution therapy. This practice finds some slight support in experiments carried out by Keller and Noble who removed the posterior lobe of the pituitary of two dogs and produced obesity.[202, 203]

The posterior lobe of the pituitary has been implicated by others because it is thought that an excess of the antidiuretic hormone may cause obesity to occur as a result of retention of water.[326] It should be pointed out that we know of no experimental studies in which obesity in animals has been produced by the injection of pituitrin, a simple proof if this theory of hyperfunction of the posterior lobe had any basis in fact.

The destruction of the pituitary occasionally results in emaciation which is known as Simmonds' cachexia,[133, 342, 356] but apparently panhypopituitarism will usually have little effect on body weight.[341] In fact, in Simmonds' original case the patient weighed 103 pounds (46.7 kg.) after ten years of illness, a weight not necessarily significant of great emaciation. Heinbecker and co-workers[171] reported that simple hypophysectomy in dogs tends to cause some gain in weight.

Kraus[214, 215] expressed the belief that there is an increase in basophils in the pituitary in constitutional obesity, and that in the four conditions of adiposis dolorosa, cerebral hyperglobulia, Morgagni-Stewart-Morel syndrome and Laurence-Moon-Biedl syndrome there is a similar increase in the basophils of the hypophysis and hyperplastic changes in the adrenals

Goldzieher[147] described histologic changes in the hypophysis in so-called "constitutional" obesity but these studies were not carried out with the cell-counting technic that Rasmussen[837] has shown to be necessary in the study of pituitary cells.

Cushing's syndrome is the one variety of obesity which is associated with pituitary disorder, and even in this instance adrenal cortical hormones probably mediate the metabolic changes responsible for the characteristic distribution of adipose tissue.

Raab[307, 308] postulates a hypophyseal hormone called "lipoitrin" which acts on the tuber cinereum to initiate neural reflexes by way of the splanchnic nerves; these reflexes, in turn, prevent the liver from taking up fat. The existence of such a mechanism has received no confirmation

Recently, Reiss[315] has associated obesity with the lactogenic hormone Because the peripheral stores of fat are reduced in lactating rats, it was thought that one effect of the lactogenic hormone might be the mobilization of fat. Reiss had observed also that the onset of obesity in some cases coincided with a failure of lactation. On this theoretical basis, lactogenic hormone of pituitary origin was administered to a number of obese patients and experimental animals. All lost weight, the loss being particularly rapid when thyroid was added to the program. This study opens a new avenue of research on the nature of obesity and requires confirmation.

Lawrence[224] has postulated a "lipopexic hormone" of pituitary origin which causes fat to be deposited in depots

A hyperactivity of the anterior lobe which changes later to hypopituitarism has been suggested as a cause of adolescent obesity.[141]

Thyroid

It is commonly but erroneously believed that myxedema and hypothyroidism without myxedema are usually associated with obesity.[86, 149, 160] However, by both animal experiments and statistical analysis of findings on myxedematous patients[244, 302] it has been well shown that hypothyroidism does not tend to cause obesity[340] Apparently the complex mechanism which regulates appetite also diminishes the intake of energy in proportion to the lowered output of energy Of course this mechanism may fail in hypothyroidism because of the patient's training, environment or neurosis just as it might fail in the euthyroid individual Then obesity would result.

Adrenals

Hyperfunction of the adrenal cortex results in either Cushing's syndrome or the adrenogenital syndrome[8] In the latter there is no characteristic obesity, but in Cushing's syndrome there is accumulation of fat about the cheeks, the supraclavicular regions, the spines of the upper thoracic and lower cervical vertebrae, and the trunk. This distribution of fat is almost diagnostic of the condition and has been noted even when the remaining portions of the body are emaciated[230, 245, 416] The glycosuria appears to result from excessive adrenal cortical hormone and is not a result of the obesity.[8, 231] This syndrome is frequently given as an example of true endocrine obesity, and there can be no argument but that the adrenocortical hormone in some way has effected a characteristic distribution of fat It is a different matter to argue that there is an invariable increase in the total amount of adipose tissue, however.[185] The patient with Cushing's disease will lose weight on a reduction diet exactly as will

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A second objection to hypoglycemia as a frequent cause for the development and maintenance of the obese state is that hypoglycemia is rarely observed in the obese but hyperglycemia is observed frequently.[283, 286] A third objection is that in the syndrome of functional hypoglycemia,[4] obesity is not mentioned as a frequent symptom, although examples of such have been reported [181, 317] In this condition there is fatigue and neurasthenia associated with low blood sugar concentrations but with no true hyperinsulinism, that is, with no islet cell tumor. In spite of the fact that the patient discovers that frequent eating may relieve his symptoms, there is often no gain in weight. The neuroses that constitute the basic part of this syndrome would be an adequate explanation for any obesity that might occur

The question of the obesity which is associated with islet cell tumors is another matter. In this condition, the hypoglycemia is so pronounced that the patient is forced to keep eating at frequent intervals to remain conscious Under such circumstances, a considerable gain in weight is usual.[404]

Gonads

It would be difficult to argue that the sex hormones have no influence on the deposition of adipose tissue It is well known to everyone that women have a pattern of fat distribution different from that of men. There is no adequate proof that there is a distinct relationship between the amount of adipose tissue and sex hormone dysfunction. The eunuch may be slender or he may be obese,[121] but so may be the individuals who are normal with respect to gonadal function; there is no proof that obesity is more frequent among persons who suffer from hypogonadism [158, 159, 354] The inconstant association of obesity and gonadectomy in human beings is to be contrasted with the obesity that usually follows gonadectomy in animals.[158] Some authors, however,

any other subject,[139] and examples of patients who had this disease but who displayed leanness have been observed.[230, 248, 416] The appearance of obesity is heightened by the osteoporosis and flattening of the vertebral bodies which shortens the neck and trunk. Ingle stated the belief that the importance of adrenal cortical hormone in the production of this syndrome has not been adequately proved,[185] but he considered Albright's hypothesis that cortical hormones may cause destruction of protein to form carbohydrates which are in turn converted to fat a good possibility.

Pancreas

One of the common symptoms of an insulin-induced hypoglycemia is hunger,[72, 279] which does not necessarily depend on the increased gastric motility and secretion[162, 183] For this reason it has been supposed that an excess supply of insulin might be responsible for ordinary obesity.[14] Serious objections can be found to this view, however. First, it is doubtful that the appetite is stimulated by hypoglycemia unless the blood sugar is lowered to shock-producing levels[16, 138, 162, 249] Apparently much of the increased intake of food during the course of insulin therapy depends on the conscious knowledge of the subject that he will have to eat heartily to avoid unpleasant symptoms Less well-controlled studies have suggested that insulin is an excellent stimulus to the production of gain in weight,[342, 343] but the powerful element of suggestion inherent in the procedure of parenteral medication appears to be an adequate explanation of its success.[138] Studies of the effects of protamine zinc and regular insulins made at the Scripps Metabolic Clinic showed that regular insulin fails to increase appetite but that protamine zinc insulin is very effective in this respect.[245, 249] The explanation offered for these contradictory findings is that rapidly developing hypoglycemia of short duration does not stimulate appetite, while long-continued and gradually increasing hypoglycemia is an effective stimulus for appetite.

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between masculine and feminine distribution of fat seems to depend on genetic as well as on hormonal factors. Rabson[809] has discussed variations in distribution of fat in obesity, and Reed and co-workers[814] have done animal experiments in this field

Another possibility is that there are nerves which have some trophic influence on the deposition and maintenance of fat[117] This will be discussed later.

Pineal body

The pineal body has an histologic appearance in childhood which suggests that it might have an endocrine function At puberty this structure undergoes degenerative changes, such as calcification, which make such function at that time unlikely This sequence of events has led to the theory that the pineal gland is one of internal secretion during childhood and that the cessation of its function leads to pubertal changes and accelerated growth[96] Some writers[94, 239] have interpreted the available evidence to mean that a hormone secreted by the pineal body itself, rather than the cessation of its formation, initiates puberty

A syndrome called "pubertas praecox" or "macrogenitosomia," which results from pineal tumors, has been described.[81] This syndrome consists of precocious sexual, physical and mental development Obesity was noted in fifteen of sixty-nine cases of pineal tumors in children reviewed by Bing, Globus and Simon. It is not certain, however, that the phenomena, such as obesity, associated with pineal tumors are not the result of hypothalamic changes due to pressure exerted by the nearby neoplasm[81] Therefore, we must conclude that obesity secondary to pineal disorders has not been proved to exist[327]

GENETIC VARIETIES

Laurence-Moon-Biedl syndrome

This consists of (1) mental deficiency, (2) retinitis pigmentosa, (3) hypogenitalism, (4) obesity and (5) poly-

have expressed the belief that hypogonadism is an important cause of obesity.[149, 387]

It has been suggested that obesity may begin more frequently at periods of gonadal change, such as puberty, pregnancy and the menopause than at other times in life,[11, 121, 149, 164, 334] and this has been taken as evidence for an endocrine nature of obesity. The shifts in hormone production in each of these periods of gonadal change are completely different, in some periods an increase and in others a decrease in the production of the various hormones concerned with sex occurs Even more complicated and varied are the changes in the production of pituitary hormone, yet it is argued that these completely different stimuli will result in the same effect, obesity. It is obvious, however, that most varieties of hypogonadism, menopause, puberty and pregnancy are associated with psychic conflicts, and it would seem likely that the joys of eating might be resorted to in compensation for the denial of other pleasures Inspection of height-weight-age tables reveals no abrupt change in the increasing incidence of obesity which occurs with advancing age, such as might be expected if menopause were an important etiologic factor

The manifestation of the presence of various hormones depends on the presence of responsive end-organs. The fact that a varying distribution of adipose tissue can occur as the result of hormonal influences is evidence that all fat cells do not respond in the same way to the same influences, that the adipose tissue of one part of the body is not entirely the same as that of the rest of the body. Hormones circulate freely in the blood, and presumably all tissues of the body are exposed to equal concentrations of them Therefore, if the fat-bearing tissues of one region of the body increase in amount in response to a change in concentration of a hormone while the adipose tissue in another part undergoes no change, there must be some difference in the adipose tissues of different regions. This difference may depend on the chromosomal influences that affect body build. Thus the difference

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Another possibility is that there are nerves which have some trophic influence on the deposition and maintenance of fat[117] This will be discussed later

Pineal body

The pineal body has an histologic appearance in childhood which suggests that it might have an endocrine function. At puberty this structure undergoes degenerative changes, such as calcification, which make such function at that time unlikely This sequence of events has led to the theory that the pineal gland is one of internal secretion during childhood and that the cessation of its function leads to pubertal changes and accelerated growth[96] Some writers[94, 239] have interpreted the available evidence to mean that a hormone secreted by the pineal body itself, rather than the cessation of its formation, initiates puberty

A syndrome called "pubertas praecox" or "macrogenitosomia," which results from pineal tumors, has been described[31] This syndrome consists of precocious sexual, physical and mental development. Obesity was noted in fifteen of sixty-nine cases of pineal tumors in children reviewed by Bing, Globus and Simon It is not certain, however, that the phenomena, such as obesity, associated with pineal tumors are not the result of hypothalamic changes due to pressure exerted by the nearby neoplasm.[31] Therefore, we must conclude that obesity secondary to pineal disorders has not been proved to exist.[327]

GENETIC VARIETIES

Laurence-Moon-Biedl syndrome

This consists of (1) mental deficiency, (2) retinitis pigmentosa, (3) hypogenitalism, (4) obesity and (5) poly-

dactyly.[223, 250, 296] It appears to be inherited in a recessive manner.[363] This syndrome was first described by Laurence and Moon in 1866 and interest in it was reawakened by reports of several cases by Bardet in 1920 and by Biedl in 1922. Biedl suggested that the syndrome could be described as dystrophia adiposogenitalis of cerebral origin. He considered that the pituitary played no part in the manifestation of the condition, but more recently a somewhat tenuous and complicated theory, which involves the concept that hypopituitarism is followed by hyperpituitarism, has been proposed by Jaso and Curbelo[189] These authors also postulate a hormone which regulates the consumption of fat. An important observation by these workers is that the obesity does not appear until after one month of age Jenkins and Poncher[190] consider that the syndrome is the result of at least three genetic characters, one causing genital dystrophy and dwarfism, a second causing retinitis pigmentosa and a third causing the skeletal anomalies such as syndactylism and polydactylism. Perhaps the most reasonable view is that presented by Warkany[395] and his co-workers which is that the syndrome is the rare chance combination of relatively frequent heredofamilial anomalies. They found that in most of the reported cases the patient did not possess all of the five cardinal symptoms and that in many cases additional anomalies were demonstrated. In summary, it can be said that the Laurence-Moon-Biedl syndrome does not appear to be endocrine in origin, that it is an ill-defined and poorly understood entity and that no proof has been advanced that the obesity results from any factor other than a large appetite and decreased activity. What may cause the increased intake of food is not known.

Morgagni-Stewart-Morel syndrome

This is perhaps better called "hyperostosis frontalis interna." It is a second rare form of obesity which is associated with inherited anomalies. It is manifested almost invariably

by internal hyperostosis of the frontal bone and by hea ache; frequently by obesity, impotence, amenorrhea, benig hypertensive cardiovascular disease, hirsutism, psychosis o psychoneurosis, fatigability and weakness; and sometime by disturbances in olfaction, Bell's palsy, diplopia and amblyopia.[161] Headache is so constant that this diagnosis should be considered in all patients complaining of cephalalgia.[212] The condition tends to be inherited in a dominant manner. Almost all of the subjects are women. Usually symptoms become disabling between the ages of forty and fifty years. Although seldom recognized, this syndrome is probably not rare. In a group of 1,620 patients who had roentgenograms of the skull for one reason or the other, 4.1 per cent were found to have the deposition of dense cancellous bone on the inner table of the frontal bone which is considered characteristic of the syndrome.[270, 271]

This entity was first described by Morgagni in 1765, and the association with insanity or neurosis was recognized by Stewart[387] in 1928 and by Morel in 1930. The latter was the first to make the diagnosis ante mortem. Many causes have been suggested and, as might be expected, the pituitary has been incriminated.[270, 273, 387] Moore[269] reported recently a case in which there was considerable cortical atrophy. On the other hand, Schneeberg and co-workers have presented rather convincing evidence that hyperostosis frontalis interna is not associated with any distinct clinical syndrome.[331a] In this condition, again there is no evidence of disturbance of fat metabolism or of endocrine dysfunction; the obesity seems to result from some derangement of the appetite-regulating mechanism.

Common familial obesity

Obesity which occurs frequently in certain families but which is not associated with other hereditary degenerative stigmas is often observed. It is the frequent plaint of the fat person that "I can't help being fat; both my parents were

Bauer[17, 354] has expressed the feeling that there is an inherited and abnormal avidity of the adipose tissue for fat which, by depriving other more vital body parts of nutrition, increases hunger and, therefore, the total intake of energy.

While we cannot, at present, state definitely the importance of heredity in obesity, we can emphasize to the patient with fat parents that he will respond to treatment in exactly the same way as will a person who has normal parents Such a patient should be told that fat is just as dangerous to him as to anyone else and that the fact that his parents were fat cannot be used as an excuse for avoidance of the necessary corrective measures.

Constitutional abnormality of adipose tissue

Lipophilia: This is a term introduced by von Bergman.[26] He expressed the belief that the adipose tissues of the fat person have a greater avidity for fat than do the tissues of the normal person and that fat is lost from these *deposits with difficulty, just as the fat in a lipoma is thought* to be retained during starvation although other fatty tissues are consumed Wells,[399] however, in his review on adipose tissue could find little evidence that, during loss of weight, the loss of fat from a benign lipoma is not in proportion to the loss from other adipose tissue. He considered that a malignant lipoma would likely retain and add to its store of fat during loss of weight, however.

Newburgh[285] expressed the belief that the obese utilize fat even more easily than do normal subjects. Two points of evidence for this view are: (1) the obese person, when losing weight, burns his fat but maintains nitrogen balance, while the starving person of normal *weight loses both protein and* fat; (2) respiratory quotients are lower in the obese than in the nonobese (see section on disorders of the use of energy). Newburgh has also been unable to find evidence for abnormalities of fat metabolism which might explain obesity. The adipose tissues of everyone seem to respond in the same way

to the stimulus of an excessive intake of energy by the laying down of predictable amounts of fat. The greater part of the synthesis of neutral fat, which forms the bulk of adipose tissue, takes place in the liver,[27, 101] but there is evidence for some formation of fat in the peripheral tissues [385]

Block [82] found no difference between obese and nonobese persons in the ease of release of fat from the adipose tissue.

A later and more complicated theory of lipophilia than that advanced by von Bergman was devised by Lichtwitz [229] He assumed that there was a decreased permeability of intracellular interphase surfaces which protect lipoid portions of the protoplasm from the action of lipase The permeability of these surfaces was thought to be regulated by both nerves and hormones

Evidence does not permit us to say that the metabolism of the adipose tissue of the obese is different from that of normal persons, the doctrine of lipophilia must be considered not proved.

Progressive lipodystrophy: This is a clinical entity which was first described by Barraquer [182] It is characterized by almost complete loss of the subcutaneous tissue of the upper half of the body and a relative or absolute obesity of the lower half The disease usually begins in childhood, occurs twice as frequently in females as in males and is compatible otherwise with good health. The cause is unknown; some relation to facial hemiatrophy and scleroderma may exist. Simons,[357] the first to use the name "lipodystrophy," expressed the belief that the nervous system, in some manner, controls the localized deposition of fat. This concept is strengthened by the sharp demarcation between areas of total loss of subcutaneous tissue and areas of excessive or normal adipose tissue which is seen in all three conditions, namely, lipodystrophy, scleroderma and facial hemiatrophy.

Beznák and Hasch[30] reported that section of the splanchnic nerves slows the rate of deposition somewhat and the rate of mobilization of fat quite markedly, so that splanch-

nicotomy results in an accumulation of perirenal fat. Similar experiments have demonstrated the effect of the autonomic nervous system on the deposition of subcutaneous and pericardial fat.[30] The importance of autonomic influences on the distribution and amount of fat in persons without neurologic lesions is impossible to state, since the anatomic interruption of nerve fibers is a distinctly abnormal condition and may cause a variety of changes not seen in common obesity. It has been postulated that the hypothalamus controls the deposition of fat at the periphery of the body by means of autonomic nerve fibers,[63] but that the experiments mentioned previously should be considered as offering no more than circumstantial evidence that regulation of the amount of fat in subcutaneous tissue is dependent on innervation is indicated by the early report of Strandberg. Strandberg grafted abdominal skin to the dorsum of the hands; when the subject later became obese, the grafted area accumulated a far greater thickness of fat than did the dorsum of the other hand.[399] This suggests that considerable control of the deposition of fat exists independently of nerve supply, but it might be interpreted also as evidence that denervation itself might cause increased deposition of fat.

As in the splanchnicotomy experiments, the studies in which the hypothalamus was injured and obesity followed are based on destructive lesions; thus, the results do not prove how important are either peripheral nerves or the hypothalamus in the day-to-day regulation of the weight of the person who does not have a neurologic lesion. The hypothalamic injury experiment finds only occasional counterpart in naturally occurring obesity, and no good examples of localized obesity due to section of peripheral nerves have come to our attention.

An endocrine theory which relates hyperthyroidism to lipodystrophy was advanced by Marañon and Soler.[347] Zon-

occurs because of a localized failure to metabolize fats,

spite of a generally increased oxidation. Lawrence[224] reported a case of lipodystrophy in a woman who had a basal metabolic rate of + 150 but in whom, after thyroidectomy, myxedema developed while the basal metabolic rate was + 40 Parmelee[287] expressed the belief that infectious or toxic influences might modify diencephalic function and, thereby, might cause lipodystrophy Ziegler[420] discussed a number of hypothetical causes and added race, heredity, alteration of fat metabolism and congenital defect to the list of possible causes He emphasized the endocrine possibilities by finding that in five of his series of seven cases some tendency toward diabetes mellitus was exhibited Hetenyi[174] found that oil injected subcutaneously into obese persons is absorbed slowly while that injected into normal persons is absorbed rapidly. He further observed that the wasted parts of a person with lipodystrophy absorb oil at a rate comparable to that in normal persons, while the obese portions of the body absorb oil slowly, as is the case in ordinary obesity. This phenomenon was interpreted as reflecting an abnormal avidity of the obese person's subcutaneous tissues for fat Another explanation, which does not resort to postulates of an anomalous metabolism of lipids, is that the injected oil is exposed to a richer supply of blood vessels in the subcutaneous tissues of a normal person than in the tissues of the obese subject and that the wider absorbing surface facilitates a more rapid diffusion into the blood

Zondek[421] has stated that limitation of diet will cause loss of weight of the obese portions of the body in lipodystrophy just as in ordinary obesity. Currier and Davis[88] reported a case of progressive lipodystrophy which appeared at the menopause, they also gave a good bibliography

In summary, progressive lipodystrophy is a poorly understood entity The striking aspect of it is not the obesity of one site but rather the wasting of the subcutaneous tissue of another.

Dercum's disease or adiposis dolorosa: This is a poorly

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In summary, progressive lipodystrophy is a poorly understood entity. The striking aspect of it is not the obesity of one site but rather the wasting of the subcutaneous tissue of another.

Dercum's disease or adiposis dolorosa: This is a poorly

understood and rarely observed syndrome characterized by tender and painful nodules of fat. The patient is said usually to be an obese woman in the latter middle life who is partly disabled by weakness and by symptoms of psychoneurosis A variety of mechanisms have been suggested for the development of this obesity, most of them endocrine.[182] There is, however, no good proof that any gland of internal secretion is at fault. Indeed, it is possible that this disease does not constitute an entity but is the chance occurrence of psychoneurosis with simple obesity. Lyon[236] considered that all gradations between simple obesity and Dercum's disease occur.

In Dercum's earlier papers,[97, 98] atrophy of the thyroid in one case and eosinophilic adenocarcinoma of the pituitary were reported. He described the fat as occurring in well-encapsulated masses and nodules. Waldorp,[386] on the other hand, expressed the belief that the condition is diencephalic in origin but based much of his opinion on the distribution of the fat, which he considered "hypophyseal." Winkelman[406] found an adenomatous hyperplasia of one adrenal gland, an adenoma of the anterior part of the pituitary and hemorrhages in the subthalamic region. He advocated a theory that the cause of the condition is a pluriglandular disturbance.

In summary, Dercum's disease has not been established as an entity and nothing of certainty is known of any cause or pathologic physiology.

DISORDERS IN THE USE OF ENERGY

Some have stated that a person can live on 400 calories per day and remain obese.[85] In well-controlled studies, however, it has been shown that obese persons must eat more than the average person in order to remain obese,[243, 284, 285, 287, 290] yet each of these persons will usually deny that he is a hearty eater.[211, 268, 282, 347]

Strang and his co-workers[370] measured the caloric in-

ht obese patients who ate as they said they ate
he average intake was 2,570 calories per day
this generous diet, the loss of weight was 0.5
: kg.) per day. Obese patients usually insist that
y little but when really adequate control has been
r dietary intake, such as is done with the patient
lic ward, loss and gain in weight have proceeded
ɔ calculation

found that relatives could frequently list the
ich obese children ate and which caused their
: intake to exceed normal or, when his confidence
, the obese child himself might admit the true
diet. Bruch observed that most mothers of
ren were very reluctant to admit that they ate
the average amount Lauter[221] noted that obese
en those whose obesity was classified as "en-
origin, consumed very large quantities of food
und that fifty obese persons ate 2,900 to 3,500
ly and still complained of hunger

xpressed the belief that all obese persons will be
e heavy eaters despite their denial[347] Evans,[282]
ig a paper by Newburgh, reported finding the
ve obese women to range up to 4,500 calories per
ch said she was a "small eater." Some capable
lieve, however, that the person with a predis-
obesity will become stout if he eats as generously
on with a tendency toward leanness who, in con-
overeat with impunity.[58, 158, 872]

as stated that the food requirement is subject to
idual variation and terms this factor the "indi-
abolic habit" This, he indicated, explains why
and some lose on the same diet[42] Presumably
olic habit depends on variability of activity, effi-
notions, basal metabolism and other less obvious
, but not on the well-studied factor of surface
e can be no argument but that some such indi-

vidual variation does occur; most of the disagreement concerns whether such differences are large enough to be of importance. It is the authors' opinion that these variations are not so large but that loss of weight can be predicted with fair accuracy if the observer is given the surface area, age, sex, occupation of the patient and the caloric value of the reduction diet.

Excessive gastro-intestinal absorption

A common but erroneous theory of obesity is that the fat person absorbs a greater proportion of the food that he eats than does the average person. This has been effectively disproved by investigations which showed that obese and normal persons absorb the same proportion of calories, nitrogen and fat from their diets.[281, 410]

"Static" obesity

Inactivity, such as that imposed by illness, immobilization by *casts and "just plain laziness," has been blamed for* obesity.[156, 287, 288] This "static" obesity is, of course, presumed to arise from a diminution in the output of energy. If the mechanism which regulates appetite were functioning normally, however, the intake of energy should diminish proportionately and the weight should remain normal. Thus, in order to explain this variety of obesity we are forced to return to psychologic, hereditary and other factors which might affect the appetite mechanism. The events (accidents, injuries and so forth) causing the inactivity may cause psychologic conflicts which, in turn, result in a normal or increased intake of food while the output of energy is diminished.

Increased efficiency in doing work

This has been postulated as a cause of obesity. *It cannot* be denied that there are variations in the amount of useless activity indulged in by different people. Some persons are

slow and careful, doing their work with a minimum of waste motion, while others accomplish the same work with considerable unnecessary motion. However, it has been convincingly demonstrated that the obese person has actually a decreased mechanical efficiency and expends extra energy to do the same work.[285, 391, 322] It is as though the extra weight of the masses of fat required just that much additional work for it to be moved about during exertion

Respiratory quotient and its vagaries

These have been intensely studied for clues to the cause of obesity The respiratory quotient is determined by dividing the intake of oxygen into the output of carbon dioxide If the subject is existing on carbohydrate alone, his respiratory quotient will be 1.0; if on protein alone, it will be 0.80; if on fat alone, it will approach 0.71. If carbohydrate is converted to fat, the quotient becomes greater than 1.0.[301] However, a similar rise in the respiratory quotient to more than unity is produced by the formation of lactic or other acids in the process of metabolism. For instance, lactic acid is formed from the fructose fraction of sucrose so that after the ingestion of table sugar, the lactic acid so formed will release carbon dioxide from the blood so that the respiratory quotient will rise to more than 1.0.[75]

Hagedorn[105] found that the postabsorptive respiratory quotient was lower in the obese than in the normal person on a carbohydrate diet and suggested that there was a qualitative anomaly in metabolism in the obese and in the potentially obese, characterized by an increased transformation of carbohydrate into fat. He found this lowering of the respiratory quotient to be proportional to the degree of overweight. Bowen and his co-workers[89] also discovered that the fasting respiratory quotient was low in the obese, but he found quotients determined after a meal of fat to be the same in normal as in the obese subjects. He also found that the specific dynamic action after the ingestion

of fat was the same in the obese as it was in normal persons. Lyon found that the respiratory quotient is low in the obese patient who is undergoing reduction of weight[235] but noted several factors, such as the carbohydrate content of the diet, which affected determination of the respiratory quotient. His findings, which parallel those of Strang, indicate that fat is being consumed at a more rapid rate in obese than in normal subjects. Krantz and Means[213] found that the respiratory quotient rises less in obese than in normal persons after injection of epinephrine and concluded that in obese persons fat is consumed preferentially to carbohydrate after injection of epinephrine. Brooks and Bridge[52] found that the respiratory quotient is elevated during the dynamic phase, that is, during that period in which weight is increasing, thus indicating the deposition of fat, but that the respiratory quotient returns nearly to normal during the static or stable phase.

It should be pointed out that determinations of the respiratory quotient are subject to considerable error and that interpretations should be made with caution. Few workers in this field have considered the rather large moment-to-moment variation in the respiratory quotient[401] and the significant effects of acid metabolic products[75] When these variations are controlled, Tepperman, Brobeck and Long[381] have stated, the finding of a respiratory quotient greater than unity means the formation of an oxygen-poor substance from one rich in oxygen Such a respiratory quotient was found by them in rats made obese by hypothalamic lesions, but it could not be said that this finding is significant of anything more than the abnormally ravenous manner in which these rats eat and their rapid deposition of fat.

In summary, it can be said that respiratory quotients exhibited by the fasting obese person tend to be somewhat lower than those of persons of normal weight, but there is no evidence that this is related to the cause of obesity. The increased caloric requirement of the obese person may tend to

exhaust carbohydrate stores more quickly and thereby cause the combustion of fat and a low respiratory quotient. There is the additional possibility that carbohydrate stores may be reduced by fatty infiltration of the liver in obesity.

Reduced specific dynamic action

This has been suggested as a cause of obesity [143, 253, 373, 387, 392, 393] The specific dynamic action is the increase in metabolism which follows the oral or parenteral administration of foods If this phenomenon were diminished, the resultant economy in loss of energy would account for a tendency to become obese The measurement of this exchange of energy is difficult, and the manner in which the exchange is expressed may alter the interpretation. If the rate of exchange is expressed as per cent of increase in basal heat production, the specific dynamic action is diminished in the obese and is raised to more than normal in the thin. However, the absolute increase in output of heat has been shown to be the same for meals of the same size and composition in persons of all weights [370] This work by Strang and McClugage conclusively rules out a diminished specific dynamic action as an explanation of obesity and shows how previous workers may have misinterpreted their findings to support such a hypothesis

It has been suggested that eating all of the day's food in one meal may diminish the specific dynamic action enough to effect an appreciable economy in loss of energy.[378]

Lauter[221] has said that the specific dynamic action is so variable that it is of little or no significance unless it can be proved to be absent. An excellent review of specific dynamic action which was prepared by Wilhelmj[414] should be studied by anyone interested in this field Goldzieher[149] stated he had demonstrated that deficiency of secretions of the anterior pituitary lobe abolishes or diminishes the specific dynamic action and thereby causes obesity in cases of hypopituitarism DuBois[108, 109] stated that an absence of specific

dynamic action would account for a saving of only 6 per cent in energy and such a saving would be trivial compared to the saving which might result from variations in activity.

In summary, it can be said that there is no good evidence that changes in the specific dynamic action are related to the cause of obesity.

Negative phase of metabolism

This was postulated by Bernhardt[28] and is closely allied to the problem of specific dynamic action. Bernhardt stated that he had demonstrated a "rebound" of metabolism in which the metabolic rate is less than the basal rate after the rise characteristic of the specific dynamic action. He indicated that the obese person would, like the normal, have a rise in the rate of metabolism after a meal (the specific dynamic action). Unlike the normal, the obese person would then undergo a fall in metabolic activity to a rate which is less than the basal rate This negative phase was thought to follow exercise also This saving in energy would then account for the obesity Wilder[411] then proved rather conclusively that this phenomenon did not occur and that Bernhardt's findings could be explained by his failure to measure basal rates accurately Others[24, 193] also have failed to demonstrate this negative phase.

Theory of "Luxus Konsumption"[152, 153]

Grafe expressed the belief that there is a mechanism in the normal person which causes an increase in metabolism after the ingestion of excess food; this increase continues until the excess of food is consumed. In this manner, the weight of the normal person would remain constant in spite of excessive intake The constitutionally obese person, however, was thought to have no such mechanism of "Luxus Konsumption" and, therefore, had no means of disposing of excess food.[152]

Lusk[222] stated that it is the condition of and not a large influx of food the previous de-

termines the basal metabolic rate Morgulis[272] associated the increase in basal metabolic rate from subnormal values, that occurs when an undernourished person is given an adequate diet, with the nitrogen retention

Keys,[210] in his studies on conscientious objectors, found that the undernourished subjects had strikingly low basal metabolic rates These rates gradually returned toward normal as the subjects approached their normal weight However, when these men were allowed to eat as they desired, they consumed enormous quantities of food and in some the basal metabolic rates became elevated considerably above normal The interpretation of these elevated rates is not immediately apparent, however; they may result simply from the specific dynamic action of the protein consumed, or perhaps from some degree of cardiac failure that may occur with the gorging of an undernourished individual Because they are observed in undernourished subjects these rates cannot be taken as proof of the doctrine of "Luxus Konsumption"

Gulick[163] stated the belief that there are thin persons who are difficult to fatten apparently because of an extravagant caloric expenditure, *but found no increase in the basal* metabolic rate from overfeeding. Wiley and Newburgh[413] found no evidence that either the total or the basal metabolism was increased by superalimentation in a thin person Johnston and Maroney,[193] in a careful study on children, demonstrated an increase in the basal metabolic rate with overfeeding which was shown to be dependent upon the increased protein intake rather than upon the increased caloric intake Rony[323] concluded that "caloric overfeeding does not cause an increase in basal metabolism unless it includes protein overfeeding."

Ketosis

This has been suspected of being a clue to the nature of obesity A greater amount of ketosis observed during the fasting of obese individuals has been thought to be related to the cause of obesity.[149, 243] Wilder has expressed the be-

lief that the phenomenon of increased ketosis may be explained by the assumption that the fat in the obese is mobilized abnormally easily or in greater quantity than in a normal person.[408] Evans and Strang[126] found that all their patients who were undergoing reduction in weight had ketonuria. MacKay and Sherrill[243] found a higher degree of ketosis in the fasting obese than in normal persons but also noted some instances of overweight in persons who exhibited no ketosis during fasting These instances of overweight they considered to be caused by deficiency of the ketogenic hormone of the anterior lobe of the pituitary, with the consequence that the fat was "locked" into storage spaces[242, 243] Folin and Denis[134] treated patients by alternating periods of starvation with periods of free choice of diet in the expectation of reduction of ketosis. They found no difference between the amount of ketogenesis in the obese and the amount in normal persons[134] On the other hand, other workers[149] have maintained that there is no ketosis during fasting in obesity DuBois has expressed the belief that fat people have an unusual resistance to the development of ketosis It has not been proved that ketogenesis in one person is quantitatively or qualitatively different from that in another if such variables as total calories, proportions of carbohydrate and fat, time of observation, exercise and degree of obesity are controlled. On the basis of such conflicting evidence as we have at hand, it is impossible to consider any of these variations in ketogenesis as proof of a metabolic error responsible for obesity

Energy changes

The energy changes involved in the constant tearing down and building up of tissues have been accused of hiding economies in loss of energy that might explain obesity.[149] Goldzieher has expressed the belief that such energy changes are beyond our means of measuring and, therefore, that all studies of energy balance are fruitless in the study of obesity This objection is easily answered by the thermodynamic ap-

proach. The formation of a large molecule from sm parts requires the same amount of energy as is release the breakdown of that molecule into those same sm parts It is contrary to all thermodynamic concepts f chemical reaction to yield more energy when going in direction than the energy absorbed when proceeding in opposite There is no reason to expect the body to viol these extensively studied and extremely well-controll thermodynamic concepts The only possible loophole here that the protoplasm of the body might have a higher conte of energy at one time than a few weeks later even thoug the protoplasm remained constant in mass This concept is highly unlikely, since it implies a fundamental change in the nature of the protoplasm from one period of observation to the next It would also account for the loss of but relatively small and definitely limited quantities of energy No one, to our knowledge, has detected such losses in any studies of energy balance

Disorder of enzymatic activity

A disorder of the enzyme system which causes oxidation of carbohydrate has been postulated According to this concept, the carbohydrate which cannot be oxidized normally is thought to be converted to fat[146] No convincing evidence has been offered in support of this theory, however

In Gierke's syndrome, obesity may develop. In this disorder there are hepatomegaly, hypoglycemia and increased stores of glycogen in many tissues of the body The syndrome is seen in the first year of life. It is thought to be caused by a failure of the enzyme system which normally allows glycogenolysis to proceed The mechanism for the production of the obesity is not apparent, however.[323]

RETENTION OF WATER

Since water constitutes the greater part of the mass of the body,[140] variations in the amount of water retained are considered by some to be a major cause of obesity in

cases.[149, 326] Because of this conception, many physicians have used diuretics of various sorts to dispose of the presumed excess of water.[158] Newburgh has demonstrated, by accurate measurements, the fluctuations in weight that may occur with variations in the store of water.[285, 290] The lag in loss of weight that frequently is observed after initiation of dietary therapy is usually caused by a temporary accumulation of water and its associated electrolytes. This water is usually excreted within a week without necessity for use of diuretics, so that loss of weight continues according to calculation.

It is well known that the loss of several pounds may occur in a normal person who is given acidifying diuretics.[251] Although Hawirko and Sprague found that the diuresis which occurred in response to administration of mersalyl (salyrgan) was much greater in the very obese subject than in the normal person,[170] a good response to treatment with diuretics cannot be taken as evidence that the obesity in a certain case is caused primarily by retention of water. It is obvious that impaired cardiac function occurring as a result of the obesity may lead to considerable increase in extracellular fluid.

The retention of water and corresponding gain of weight that precedes each menstrual period in many women appears to be caused by a rise in the level of estrogens at that time. Since estrogens like desoxycorticosterone acetate appear to cause retention of water, an "endocrine" form of obesity in which the increase in weight is due to retention of water has been postulated The retention of water in myxedema is well relieved by administration of thyroid extract;[302] for this reason thyroid extract has been used with questionable success as a diuretic in obese persons with normal metabolism The influence of the posterior lobe of the hypophysis and of the adrenal cortex on water balance suggests to some investigators that obesity may arise as a result of the increased function of those glands[149] But in spite of all these at-

tempts to relate dysfunction of the thyroid, pituitary, adrenal cortex and ovary to obesity by way of their effect on water balance, no one has proved that more than ten to fifteen pounds (4 5 to 6 8 kg.) of excess fluid may be present without pitting edema. This attempt to link hormones with obesity by way of water balance fails because no one has demonstrated that obesity can result primarily from retention of water In all commonly seen examples of water retention, such as occurs in nephritis, cardiac failure and intoxication from desoxycorticosterone acetate, pitting edema gives early evidence of the excess water and no obesity occurs

Goldzieher expressed the belief that the water accumulated in obesity is intracellular,[149] but gave no proof. It is conceivable that an increase in the content of intracellular water might cause no edema, while a similar increase in extracellular fluid might do so, but no one to our knowledge has given adequate proof that there exists such a syndrome of increased volume of intracellular fluid as a cause of obesity.

Chapter IV

CONTRAINDICATIONS TO REDUCTION

CONTRAINDICATIONS to reduction are extremely rare and possibly may not exist, but situations which demand caution and a slower rate of reduction are not infrequently met.

Active or recently active tuberculosis is frequently cited as an absolute contraindication to reduction.[409] This problem is not met frequently, since most such patients are not well nourished. There is convincing evidence that the malnutrition which accompanies war will increase the incidence of tuberculosis[318] but the thesis that properly supervised reduction of excess weight to normal will possibly activate a latent tuberculosis has not been proved. There is little data available concerning obesity in tuberculosis, but one opinion is that tuberculosis develops in fewer obese persons than in those of normal weight; however, once the infection is present, its course in the obese is no different from that in the person of normal weight.[316] Overfeeding as therapy for tuberculosis has been advised against.[287]

The importance of a generous supply of carbohydrate and protein in the treatment of cirrhosis has been emphasized.[85, 133] The obese person subsisting on a 600 calorie diet is actually metabolizing a mixture which is composed principally of fat (derived chiefly from his own body) and which contains relatively small amounts of protein and carbohydrate (derived entirely from the diet). It is reasonable to assume, therefore, that rigorous dieting would have an adverse effect on the cirrhotic process and that if reduction of weight becomes urgent in such cases it should be accomplished slowly. Actually this problem arises only occasion-

ally, since many patients with cirrhosis have lost weight as a result of their disease

An active duodenal or gastric ulcer is a contraindication to any considerable restriction of diet In such cases the program should provide for only a slow loss of weight and for the inclusion of foods in the diet which are appropriate to therapy of ulcer. Antacids would play a major part in such a program.

A diet low in purines and adequate in protein is difficult to devise unless it contains 1,500 calories or more. For this reason, reduction should proceed slowly in patients with gout.

Since chronic ulcerative colitis usually causes considerable emaciation, it is usually wise to keep such patients somewhat overweight, if possible

Addison's disease is a reason for slow reduction since compensatory mechanisms of many sorts, including the process of gluconeogenesis, are impaired and a too rigorously limited diet might precipitate hypoglycemia or even an addisonian crisis Obesity in Addison's disease, as in tuberculosis, is unusual, however.

The presence of an inoperable malignant tumor or lymphoblastoma in which cachexia is likely to develop should make one less concerned about lesser grades of obesity and better satisfied with the slower rates of loss which may be obtained by simple warnings that the intake of food be limited somewhat when the patient is exceedingly obese

Age is no bar to reduction of weight. It has been stated that children and old people bear reduction of weight poorly,[394] but we have been unable to find any basis for this belief. It is particularly necessary to supply growing children and pregnant women with all essential food elements, but properly designed reduction diets accomplish this. Evans[125] has pointed out that obesity in children is frequently complicated by emotional difficulties, sometimes

termed "behavior problems;" too great a restriction of food may precipitate further disciplinary crises in such circumstances and as a consequence, Evans has expressed the belief that the pediatrician may have to evaluate the emotional situation carefully before subjecting a child to a rigorous dietary program

In elderly persons whose life expectancy is not great and whose ability to learn a strict diet is limited, one may again have to be satisfied with simpler and less effective programs, but the benefits of reduction of weight in the elderly obese are great and the physician's efforts frequently will be well rewarded by a considerable improvement in the health of these persons.

Coronary artery disease and hypertension are sometimes given as contraindications to reduction,[19] but rather they should be considered as urgent reasons for the procedure There is no reason to expect cardiac catastrophes to follow reduction in persons with coronary artery disease.

The danger that acidosis might result from starvation ketogenesis was mentioned in earlier studies,[19, 122, 208] but such has not been demonstrated to be of significance in properly devised programs of reduction.

Once reduction is well under way, it is necessary to decide how far the procedure should be carried. Should we attempt to tailor the patient exactly to the weight given in standard height-weight tables? This is a decision which must be made by the physician in each individual case; he may justifiably halt the program fifteen to twenty pounds (6 8 to 9.1 kg.) short of the goal if the ends have been achieved, or, in some instances, he may find it wise to reduce the weight below that given by the standard tables as ideal for the patient. The latter situation may arise in the treatment of cardiac decompensation or coronary artery disease in which undernutrition may reduce the work of the heart 33 to 49 per cent and thus may diminish or abolish symptoms which might otherwise be manifest.[255, 257]

Chapter V

DIETS FOR OBESITY

ALICE KARSLAKE IRMISCH

WHILE there is much disagreement about other therapeutic measures, nearly every worker in this field agrees that restriction of food is the most important factor in the reduction of weight There is now rather general agreement that the diet should contain an adequate supply of protein, a minimum of fat, enough carbohydrate to prevent wasting of protein and an adequate supply of vitamins and minerals

The first recorded diet for obesity in the literature is that of William Banting[1] of London in 1863 William Harvey restricted the carbohydrate and fat intake of this patient which resulted in a loss of forty-six pounds (20 9 kg). In 1915, Folin and Denis[184] recommended five days of starvation, repeated at intervals, as a safe and harmless treatment of obesity Evans and his co-workers have published what is probably the most thorough discussion of diets for obesity. In 1929 they[126] reported the use of a 600 to 700 calorie diet on ninety-eight patients The average loss of weight was twenty-six pounds (11.8 kg.). They predicted the amount of loss by calculating the caloric requirement (present weight, in kilograms, multiplied by 30 calories per kilogram) and subtracting the caloric intake, the result of which gave the caloric deficit; this result was divided by 9 to obtain the value for grams of fat lost, and this value was increased by 14 per cent to obtain the value for grams of fatty tissue lost per day

In 1930 Strang, McClugage and Evans[370] gave diets even lower in calories They used only lean protein foods, with

either 100 gm. of milk or orange juice containing 50 c.c. of yeast. This diet provided, on the average, 58 gm of protein and only 360 calories. The thirteen patients treated showed an average loss in weight of 0.6 pounds (0.3 kg.) per day for fifty-nine days. All were benefited clinically, with no evidence of acidosis This is the first mention of the addition of vitamin preparations to low calorie diets. In 1931 the same authors[871] added viosterol as well as yeast A 335 calorie diet[127] given to 187 obese patients resulted in an average loss of thirty pounds (13 6 kg.) in eight or nine weeks Although a loss of nitrogen averaging 2 gm per day was encountered, the fact that the creatinine coefficient underwent little change was thought to indicate that fat, mainly, rather than protein, was lost.[238] The patients found the almost exclusively protein diet impalatable after a few weeks, so that 20 gm. of carbohydrate were added in the form of fruits and vegetables. The diet was much more palatable and only 0 1 gm. of nitrogen was lost per day, which is negligible. Keeton and Dickson[201] followed the

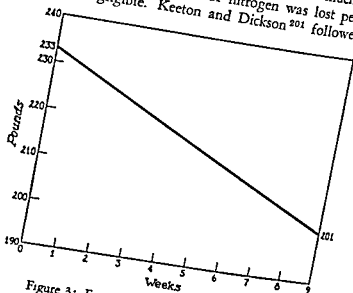


Figure 3· Example of case given in Table VII

nitrogen balance of obese patients on low calorie diets (1,024 to 1,600 calories) with a protein content varying from 13.5 to 90 gm. Even on the low protein intake, the loss of nitrogen was small. It was found that nitrogen balance could be maintained, in the reduction of an obese person, so long as 1 gm. of protein per kilogram of ideal body weight was supplied daily, although early in the reducing program there tended to be a negative balance, perhaps because of the consumption of protein for its antiketogenic properties.[371]

Brown, Herman and Ohlson[69] found that when obese women of college age subsisted on reduction diets of 1,000 to 1,200 calories, they remained in approximate nitrogen, calcium and phosphorus equilibrium. These authors were concerned that appreciable positive balances of these minerals were not observed, thus implying that reduction diets might impair the health of persons of college age It would seem, however, that this group would have attained the major portion of their growth, and easily measurable positive balances of nitrogen, calcium and phosphorus should not occur. The greater the initial weight, the less the rate of nitrogen loss on a deficient diet[352]

Grafe[152] expressed the thought that the American low calorie diets were too rigorous for Europeans. He considered a 984 calorie diet to be minimal. As in many other instances, his diets do not include milk A 500 calorie diet similar to those used by Evans and co-workers was given to obese patients by Wilder[408] with success Wilder has developed a formula[409] for predicting the loss of weight on a given caloric level The derivation of his method, its practical application and examples of its use may be found in Tables VII through XI and Figs 3 through 9 A chart of the predicted loss in weight is advantageous both to the patient and to the doctor. It is a guide to indicate how much weight the patient may be expected to lose every week on a given caloric intake If the actual loss approximates the predicted one, the patient is encouraged If he does not lose as ex-

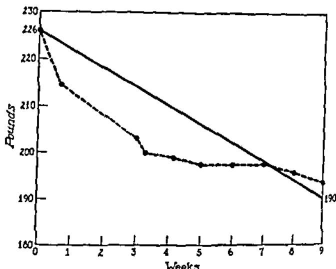


Figure 4 Calculation of predicted weight loss for a fifty-three year old man, 67 25 inches in height, weighing 226 pounds· basal calories for 195 pounds, 1,740; basal calories plus 50 per cent, 2,610; caloric intake, 620, caloric deficit, 1,990; predicted average weight loss per week, 4 0 pounds, or 36 pounds for the nine week period. The actual loss was 33 pounds in nine weeks, the final weight being 193 pounds. (The solid line represents the predicted weight loss, the broken line, the actual weight loss)

pected, the physician is more careful to inquire as to the patient's intake of food so as to determine whether or not there is any discrepancy or variation. Perhaps the weight is due to a retention of water which will disappear after another week or two on the same regimen. Patients who carefully adhere to a low calorie diet in detail inevitably lose weight

Figures 4 to 9 inclusive demonstrate the response of a number of patients to dietary therapy. The solid lines indicate the weight loss that was predicted for the patient at the beginning of each nine week period of therapy. In practice, we give the patient a graph similar to these with the line of the predicted weight loss drawn in place The patient then charts his actual weight at intervals of two to seven days

Near the end of the nine week period the patient is given a second graph which shows the predicted rate of weight loss for the next period. As many as four or five graphs for succeeding nine week periods may be computed for the very obese patient.

There are two reasons for recalculating the predicted rate of weight loss periodically rather than for the entire course of reduction at the initiation of therapy First, the rate of weight loss is rapid in the earlier weeks and becomes gradually slower as the patient's surface area becomes less This phenomenon is demonstrated in Figures 7, 8 and 9, where the predicted rate of weight loss becomes less with each succeeding period Second, the use of the actual rather than predicted weight at the beginning of each nine week period prevents a cumulative deviation from the predicted line (Fig 7)

An amazingly close correlation of predicted and actual weight loss is shown in Figure 8. It seems reasonable that the patient who discovers that he is a few pounds "ahead of schedule" may exceed his diet slightly, and the patient who is not losing quite as rapidly as predicted will adhere to his diet with increased determination, thus tailoring his actual weight loss to fit the predicted one

It is our belief that such graphs of predicted weight loss are a real factor in helping the patient adhere to his dietary program and should be included in reduction programs which utilize the 620 calorie diet

Anderson developed a formula somewhat similar to that of Wilder's, and with it demonstrated a close relation between weight loss and caloric deficit [8] He found diets high in fat to cause weight loss at rates equal to those produced by high carbohydrate diets if the caloric deficit were kept constant.

Mulier and Topper [275] in 1934, reported on the treatment of obesity in a group of twenty-five children, many of whom had a basal metabolic rate which was somewhat greater than

TABLE VII

Method of Predicting Weight Loss

1. Determine the basal energy requirement using the Boothby and Berkson Food Nomogram (Fig. 10).[16] The ideal or normal weight is used for the calculation unless the patient is more than 50 pounds (22.7 kg) overweight. When actual weight exceeds the standard weight by 50 pounds, the energy requirement [illegible] figure represents the total calorie requirement.
2 The difference between the calorie requirement and the calorie intake is termed the "calorie deficit." This figure multiplied by the factor .002* will give the loss of weight per week in pounds
3. A graph can be constructed by plotting the curve of predicted weight loss from day to day (Fig. 3).
Example: The calculation for a woman who is thirty-six years old, whose height is 63 inches (160 cm), whose weight is 233 pounds [illegible]

* The factor .002 is obtained as follows D (calorie deficit) divided by 9.3 gives the grams of fat lost per day The grams of fat lost per day multiplied by the factor $\frac{100}{86}$ gives the grams of weight lost per day, where fat tissue contains 14 per cent of water Grams of weight lost per day multiplied by 7 gives the grams of weight lost per week. The grams of weight lost per week multiplied by the factor $\frac{2.2}{1000}$ gives the pounds lost per week.

Thus, the pounds lost per week $= \frac{D}{9.3} \times \frac{100}{86} \times 7 \times \frac{2.2}{1000} = D \times 0.00193$,

or approximately $D \times .002$.

normal. The intake of calories was reduced and the form of protein eaten was chiefly that of meat, fish, cheese and eggs A limited amount of milk was allowed the younger children Fluids were restricted to 500 to 600 c c. and salt to 0.3 gm daily. Restriction of fluids and salt is common in many dietary programs for obesity,[17] but is ordinarily unnecessary and undesirable. Doubtless some patients fail to lose weight

TABLE VIII

Height—Weight—Age Table (Boys) * †

Height inches	5 yrs.	6 yrs	7 yrs	8 yrs	9 yrs.	10 yrs.	11 yrs	12 yrs	13 yrs	14 yrs	15 yrs	16 yrs	17 yrs	18 yrs	19 yrs
38	34	34													
39	35	35													
40	36	36													
41	38	38	38												
42	39	39	39	39											
43	41	41	41	41											
44	44	44	44	44											
45	46	46	46	46	46										
46	47	48	48	48	48										
47	49	50	50	50	50	50									
48		52	53	53	53	53									
49		55	55	55	55	55	55								
50		57	58	58	58	58	58	58							
51			61	61	61	61	61	61							
52			63	64	64	64	64	64	64						
53			66	67	67	67	67	68	68						
54				70	70	70	70	71	71	72					
55				72	72	73	73	74	74	74					
56				75	76	77	77	77	78	78	80				
57					79	80	81	81	82	83	83				
58					83	84	84	85	85	86	87				
59						87	88	89	89	90	90	90			
60						91	92	92	93	94	95	96			
61							95	96	97	99	100	103	106		
62							100	101	102	103	104	107	111	116	
63							105	106	107	108	110	113	118	123	127
64								109	111	113	115	117	121	126	130
65								114	117	118	120	122	127	131	134
66									119	122	125	128	132	136	139
67									124	128	130	134	136	139	142
68										134	134	137	141	143	147
69										137	139	143	146	149	152
70										143	144	145	148	151	155
71										148	150	151	152	154	159
72											153	155	156	158	163
73											157	160	162	164	167
74											160	164	168	170	171

* When taking measurements, remove the outdoor clothing, shoes and coat Age is taken to the last birthday

† From Wilder, R. M *A primer for diabetic patients. Ed. 7,* Philadelphia, W B Saunders Company, 1941

consistently because of water retention, but this is a temporary condition, and continuance on the low calorie diet will eventually produce the predicted loss of weight.

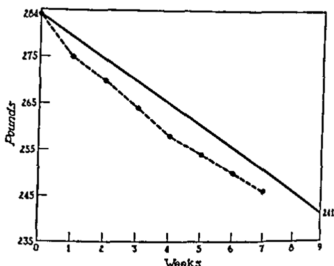


Figure 5· Calculation of predicted weight loss for a forty-one year old man, 67 5 inches in height, weighing 284 pounds: basal calories for 254 pounds, 2,020; basal calories plus 50 per cent, 3,030, caloric intake, 620, caloric deficit, 2,410; predicted average weight loss per week, 4 8 pounds, or 32 6 pounds for seven weeks The actual loss was 38 pounds in seven weeks, the final weight being 246 pounds (The solid line represents the predicted weight loss, the broken line, the actual weight loss)

In 1938 McCullagh[240] reported the use of an 800 calorie diet for patients with obesity. For the first time, the importance of adequate intake of minerals, as well as of protein and vitamins, was stressed He stated that it might be advisable to prescribe calcium gluconate tablets, as well as yeast and vitamins A and D, and to include in the diet not only lean meat, cottage cheese and one egg but also two glasses of milk. Most other reduction diets include only one glass of milk, or even less, although Kemper,[206] in 1940, gave two teaspoonfuls of dibasic calcium phosphate to his

TABLE IX

HEIGHT—WEIGHT—AGE TABLE (GIRLS) * †

Height inches	5 yrs	6 yrs.	7 yrs.	8 yrs.	9 yrs	10 yrs.	11 yrs.	12 yrs.	13 yrs.	14 yrs	15 yrs.	16 yrs	17 yrs	18 yrs.
38	33	33												
39	34	34												
40	36	36	36											
41	37	37	37											
42	39	39	39											
43	41	41	41	41										
44	42	42	42	42										
45	45	45	45	45	45									
46	47	47	47	48	48									
47	49	50	50	50	50	50								
48		52	52	52	52	53	53							
49		54	54	55	55	56	56							
50		56	56	57	58	59	61	62						
51			59	60	61	61	63	65						
52			63	64	64	64	65	67						
53			66	67	67	68	68	69	71					
54				69	70	70	71	71	73					
55				72	74	74	74	75	77	78				
56					76	78	78	79	81	83				
57					80	82	82	82	84	88	92			
58						84	86	86	88	93	96	101		
59						87	90	90	92	96	100	103	104	
60						91	95	95	97	101	105	108	109	111
61							99	100	101	105	108	112	113	116
62							104	105	106	109	113	115	117	118
63								110	110	112	116	117	119	120
64								114	115	117	119	120	122	123
65								118	120	121	122	123	125	126
66									124	124	125	128	129	130
67									128	130	131	133	133	135
68									131	133	135	136	138	138
69										135	137	138	140	142
70										136	138	140	142	144
71										138	140	142	144	145

* When taking measurements, remove the outdoor clothing, shoes and coat. Age is taken to the last birthday

† From Wilder, R. M *A primer for diabetic patients* Ed 7, Philadelphia, W. B. Saunders Company, 1941

TABLE X

AVERAGE HEIGHT—WEIGHT—AGE TABLE (MEN) * †

Graded average weight

Age	5 ft.	5 ft. 1 in	5 ft. 2 in	5 ft. 3 in	5 ft. 4 in.	5 ft. 5 in.	5 ft. 6 in	5 ft 7 in.	5 ft. 8 in	5 ft. 9 in.	5 ft. 10 in	5 ft 11 in	6 ft.	6 ft. 1 in.	6 ft. 2 in.	6 ft. 3 in.	6 ft. 4 in.	6 ft. 5 in
15	107	109	112	115	118	122	126	130	134	138	142	147	152	157	162	167	172	177
16	109	111	114	117	120	124	128	132	136	140	144	149	154	159	164	169	174	179
17	111	113	116	119	122	126	130	134	138	142	146	151	156	161	166	171	176	181
18	113	115	118	121	124	128	132	136	140	144	148	153	158	163	168	173	178	183
19	115	117	120	123	126	130	134	138	142	146	150	155	160	165	170	175	180	185
20	117	119	122	125	128	132	136	140	144	148	152	156	161	166	171	176	181	186
21	118	120	123	126	130	134	138	141	145	149	153	157	162	167	172	177	182	187
22	119	121	124	127	131	135	139	142	146	150	154	158	163	168	173	178	183	188
23	120	122	125	128	132	136	140	143	147	151	155	159	164	169	175	180	185	190
24	121	123	126	129	133	137	141	144	148	152	156	160	165	171	177	182	187	192
25	122	124	126	129	133	137	141	145	149	153	157	162	167	173	179	184	189	194
26	123	125	127	130	134	138	142	146	150	154	158	163	168	174	180	186	191	196
27	124	126	128	131	134	138	142	146	150	154	158	163	169	175	181	187	192	197
28	125	127	129	132	135	139	143	147	151	155	159	164	170	176	182	188	193	198
29	126	128	130	133	136	140	144	148	152	156	160	165	171	177	183	189	194	199
30	126	128	130	133	136	140	144	148	152	156	161	166	172	178	184	190	196	201
31	127	129	131	134	137	141	145	149	153	157	162	167	173	179	185	191	197	202
32	127	129	131	134	137	141	145	149	154	158	163	168	174	180	186	192	198	203
33	127	129	131	134	137	141	145	149	154	159	164	169	175	181	187	193	199	204
34	128	130	132	135	138	142	146	150	155	160	165	170	176	182	188	194	200	206

TABLE X — *Continued*

35	128	130	132	135	138	142	146	150	155	160	165	170	176	182	189	07
36	129	131	133	136	139	143	147	151	156	161	166	171	177	183	190	08
37	129	131	133	136	140	144	148	152	157	162	167	172	178	184	191	09
38	130	132	134	137	140	144	148	152	157	162	167	173	179	185	192	10
39	130	132	134	137	140	144	148	152	157	162	167	173	179	185	192	11
40	131	133	135	138	141	145	149	153	158	163	168	174	180	186	193	12
41	131	133	135	138	141	145	149	153	158	163	168	174	180	186	193	13
42	132	134	136	139	142	146	150	154	159	164	169	175	181	187	194	14
43	132	134	136	139	142	146	150	154	159	164	169	175	181	187	194	14
44	133	135	137	140	143	147	151	155	160	165	170	176	182	188	195	15
45	133	135	137	140	143	147	151	155	160	165	170	176	182	188	195	15
46	134	136	138	141	144	148	152	156	161	166	171	177	183	189	196	16
47	134	136	138	141	144	148	152	156	161	166	171	177	183	190	197	17
48	134	136	138	141	144	148	152	156	161	166	171	177	183	190	197	17
49	134	136	138	141	144	148	152	156	161	166	171	177	183	190	197	17
50	134	136	138	141	144	148	152	156	161	166	171	177	183	190	197	17
51	135	137	139	142	145	149	153	157	162	167	172	178	184	191	198	18
52	135	137	139	142	145	149	153	157	162	167	172	178	184	191	198	18
53	135	137	139	142	145	149	153	157	162	167	172	178	184	191	198	18
54	135	137	139	142	145	149	153	158	163	168	173	178	184	191	198	19
55 and up	135	137	139	142	145	149	153	158	163	168	173	178	184	191	198	19

* When taking measurements, remove the outdoor clothing, shoes and coat Age is taken to the

† From Wilder, R. M *A primer for diabetic patients* Ed 7, Philadelphia, W B Saunders Co

TABLE XI

AVERAGE HEIGHT—WEIGHT—AGE TABLE (WOMEN) * †

Graded average weight

Age	4 ft. 8 in.	4 ft 9 in	4 ft 10 in	4 ft. 11 in	5 ft.	5 ft 1 in.	5 ft. 2 in.	5 ft 3 in.	5 ft 4 in.	5 ft 5 in.	5 ft. 6 in.	5 ft 7 in	5 ft. 8 in.	5 ft. 9 in	5 ft. 10 in.	5 ft. 11 in	6 ft.
15	101	103	105	106	107	109	112	115	118	122	126	130	134	138	142	147	152
16	102	104	106	108	109	111	114	117	120	124	128	132	136	139	143	148	153
17	103	105	107	109	111	113	116	119	122	125	129	133	137	140	144	149	154
18	104	106	108	110	112	114	117	120	123	126	130	134	138	141	145	150	155
19	105	107	109	111	113	115	118	121	124	127	131	135	139	142	146	151	155
20	106	108	110	112	114	116	119	122	125	128	132	136	140	143	147	151	156
21	107	109	111	113	115	117	120	123	126	129	133	137	141	144	148	152	156
22	107	109	111	113	115	117	120	123	126	129	133	137	141	145	149	153	157
23	108	110	112	114	116	118	121	124	127	130	134	138	142	146	150	153	157
24	109	111	113	115	117	119	121	124	127	130	134	138	142	146	150	154	158
25	109	111	113	115	117	119	121	124	128	131	135	139	143	147	151	154	158
26	110	112	114	116	118	120	122	125	128	131	135	139	143	147	151	155	159
27	110	112	114	116	118	120	122	125	129	132	136	140	144	148	152	155	159
28	111	113	115	117	119	121	123	126	130	133	137	141	145	149	153	156	160
29	111	113	115	117	119	121	123	126	130	133	137	141	145	149	153	156	160
30	112	114	116	118	120	122	124	127	131	134	138	142	146	150	154	157	161
31	113	115	117	119	121	123	125	128	132	135	139	143	147	151	154	157	161
32	113	115	117	119	121	123	125	128	132	136	140	144	148	152	155	158	162
33	114	116	118	120	122	124	126	129	133	137	141	145	149	153	156	159	162
34	115	117	119	121	123	125	127	130	134	138	142	146	150	154	157	160	163

TABLE XI — *Continued*

35	115	117	119	121	123	125	127	130	134	138	142	146	150	154	157	160	163
36	116	118	120	122	124	126	128	131	135	139	143	147	151	155	158	161	164
37	116	118	120	122	124	126	129	132	136	140	144	148	152	156	159	162	165
38	117	119	121	123	125	127	130	133	137	141	145	149	153	157	160	163	166
39	118	120	122	124	126	128	131	134	138	142	146	150	154	158	161	164	167
40	119	121	123	125	127	129	132	135	138	142	146	150	154	158	161	164	167
41	120	122	124	126	128	130	133	136	139	143	147	151	155	159	162	165	168
42	120	122	124	126	128	130	133	136	139	143	147	151	155	159	162	166	169
43	121	123	125	127	129	131	134	137	140	144	148	152	156	160	163	167	170
44	122	124	126	128	130	132	135	138	141	145	149	153	157	161	164	168	171
45	122	124	126	128	130	132	135	138	141	145	149	153	157	161	164	168	171
46	123	125	127	129	131	133	136	139	142	146	150	154	158	162	165	169	172
47	123	125	127	129	131	133	136	139	142	146	151	155	159	163	166	170	173
48	124	126	128	130	132	134	137	140	143	147	152	156	160	164	167	171	174
49	124	126	128	130	132	134	137	140	143	147	152	156	161	165	168	172	175
50	125	127	129	131	133	135	138	141	144	148	152	156	161	165	169	173	176
51	125	127	129	131	133	135	138	141	144	148	152	157	162	166	170	174	177
52	125	127	129	131	133	135	138	141	144	148	152	157	162	166	170	174	177
53	125	127	129	131	133	135	138	141	144	148	152	157	162	166	170	174	177
54	125	127	129	131	133	135	138	141	144	148	153	158	163	167	171	174	177
55	125	127	129	131	133	135	138	141	144	148	153	158	163	167	171	174	177

* When taking measurements, remove the outdoor clothing, shoes and coat. Age is taken to the last birthday.

† From Wilder, R. M. *A primer for diabetic patients* Ed 7, Philadelphia, W. B. Saunders Company, 1941

TABLE XII

Low Calorie Diets

		600 calorie	1,000 calorie	Special 1,200 calorie	1,500 calorie	Recommended allowances, normal range*	
						Women	Men
Vegetable 3%	gm.	*300*	400	400	400		
Vegetable 20%	gm				100		
Fruit 5%	gm.	200					
Fruit 10%	gm.	100	300	300	200		
Fruit 25%	gm.				*100*		
Bread	gm.	10	60	40	60		
Cream 20%	gm.		30	30	30		
Milk, skimmed	gm.	400	480	960			
Milk, whole	*gm.*				*480*		
Eggs, each	gm.	1	1	1	1		
Meat, very lean	gm.	150	150	150			
Meat, lean	gm.				150		
Butter	gm.		15	15	25		
Approximate composition:							
Carbohydrate	gm.	*55*	*100*	*115*	*135*		
Protein	gm	60	70	85	75	60	70
Fat	gm	15	40	45	75		
Calories		620	1,030	1,180	1,510	2,500	3,000
Calcium	*mg.*	*660*	*870*	*1,420*	880	800	800
Iron	mg	9	11	11	12	12	0
Vitamin A	I.U.	2,400	6,200	6,000	7,300	5,000	5,000
Thiamine	mg	1 1	1.5	1 6	1 6	1 2	1 5
Riboflavin	mg.	1 4	1.7	2 6	1 8	1 6	2 0
Niacin	mg.	10	12	11	13	12	15
Ascorbic acid	mg	120	160	160	170	70	75

* *Recommended dietary allowances,* National Research Council, Reprint and Circular Series, No. 122, August, 1945.[**]

probably has little effect on the satiety value If the patient becomes constipated, bulk may be added by medication. Bran is no longer in common use because of its tendency to irritate the large bowel Mineral oil, whether used as a laxative or as an ingredient in cooking, is also in disfavor because of the increased excretion of the fat-soluble vitamins following its use.

Once the patient attains the desired weight, attention to the diet must not be abandoned, since unrestricted feeding will often cause the weight to return to its original figure.[111] Therefore, a moderately restricted diet, usually measured rather than weighed, of 1,500 to 1,800 calories should be prescribed Patients will usually eat a little more than this, thereby actually consuming about 20 to 40 per cent more than their basal requirement Such a diet should maintain their weight constant at a desirable level, but if not, the periodic return to a more rigorous diet may be necessary.

Fellows[131] showed that five years after a successful loss of weight, 79 per cent of a group of patients had regained all or part of their lost weight Rony has emphasized that the once obese person must be constantly on guard to prevent gain of weight, since the body weight-regulating mechanism scarcely ever seems to regain an entirely normal function

Sample low calorie diets are included in Tables XII, XIII and XIV. Other caloric levels than these also may be used Diets of 600 or 800 calories are always weighed in grams whether served at home or in the hospital Other low calorie diets may be weighed or measured as the circumstances indicate. Every patient should be instructed in his diet individually, in a series of lessons, including a lesson on the adequate diet, one on the supplements necessary in a low calorie diet, one on the menu plan for his individual diet and one or two lessons in menu planning by use of various substitutions, including not only menus of equal caloric value but also those of equal carbohydrate, protein

TABLE XII

Low Calorie Diets

		600 calorie	1,000 calorie	Special 1,200 calorie	1,500 calorie	Recommended allowances, normal range*	
						Women	Men
Vegetable 3%	gm.	300	400	400	400		
Vegetable 20%	gm				100		
Fruit 5%	gm	200					
Fruit 10%	gm.	100	300	300	200		
Fruit 25%	gm.				100		
Bread	gm.	10	60	40	60		
Cream 20%	gm.		30	30	30		
Milk, skimmed	gm	400	480	960			
Milk, whole	gm				480		
Eggs, each	gm.	1	1	1	1		
Meat, very lean	gm	150	150	150			
Meat, lean	gm.				150		
Butter	gm.		15	15	25		
Approximate composition.							
Carbohydrate	gm.	55	100	115	135		
Protein	gm	60	70	85	75	60	70
Fat	gm.	15	40	45	75		
Calories		620	1,030	1,180	1,510	2,500	3,000
Calcium	mg.	660	870	1,420	880	800	800
Iron	mg	9	11	11	12	12	0
Vitamin A	I U.	2,400	6,200	6,000	7,300	5,000	5,000
Thiamine	mg.	1.1	1.5	1.6	1.6	1.2	1.5
Riboflavin	mg	1.4	1.7	2.6	1.8	1.6	2.0
Niacin	mg	10	12	11	13	12	15
Ascorbic acid	mg	120	160	160	170	70	75

* *Recommended dietary allowances,* National Research Council, Reprint and Circular Series, No. 122, August, 1945.[300]

probably has little effect on the satiety value. If the patient becomes constipated, bulk may be added by medication Bran is no longer in common use because of its tendency to irritate the large bowel. Mineral oil, whether used as a laxative or as an ingredient in cooking, is also in disfavor because of the increased excretion of the fat-soluble vitamins following its use

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Fellows [131] showed that five years after a successful loss of weight, 79 per cent of a group of patients had regained all or part of their lost weight. Rony has emphasized that the once obese person must be constantly on guard to prevent gain of weight, since the body weight-regulating mechanism scarcely ever seems to regain an entirely normal function.

Sample low calorie diets are included in Tables XII, XIII and XIV Other caloric levels than these also may be used Diets of 600 or 800 calories are always weighed in grams whether served at home or in the hospital Other low calorie diets may be weighed or measured as the circumstances indicate. Every patient should be instructed in his diet individually, in a series of lessons, including a lesson on the adequate diet, one on the supplements necessary in a low calorie diet, one on the menu plan for his individual diet and one or two lessons in menu planning by use of various substitutions, including not only menus of equal caloric value but also those of equal carbohydrate, protein

and fat value (Tables XV, XVI, XVII and XVIII). Non-caloric fluids, such as broth, tea and coffee, are actually unlimited. "Per cent" refers to per cent of carbohydrate, except in the case of cream, in which case the per cent of fat is indicated.

Four diets are given herein, with the approximate composition of a typical menu, and one menu is given for each diet (Tables XIII and XIV). Many more could be devised easily by use of the food tables. The special 1,200 calorie diet is included for use with patients who require a quart of

TABLE XIII

SAMPLE MENU FOR LOW CALORIE DIETS

	600 calorie		1,000 calorie	
	Food	Weight, gm.	Food	Weight, gm.
Breakfast				
10% fruit	Grapefruit	100	Grapefruit	100
Egg	Egg, soft cooked	one	Egg, soft cooked	one
Bread, toasted	Whole wheat toast	10	Whole wheat toast	20
Butter			Butter	5
20% cream			20% cream	30
Beverage	Coffee	1 cup	Coffee	1 cup
Dinner				
Soup	Broth	1 cup	Broth	1 cup
Lean meat	Lean roast beef	75	Lean roast beef	75
3% vegetable	New cabbage	75	New cabbage	100
3% vegetable	Tomato salad	75	Tomato salad	100
5% fruit	Water packed peaches	100		
10% fruit			Orange slices	100
Skimmed milk	Skimmed milk	200	Skimmed milk	240
Bread			Whole wheat bread	20
Butter			Butter	5
Supper				
Lean meat	Lean sliced ham	75	Lean sliced ham	75
3% vegetable	Green beans	100	Green beans	100
3% vegetable	Celery sticks	50	Celery and	50
			carrot sticks	25
10% fruit	Water packed pears	50	Water packed pears	100
Skimmed milk	Skimmed milk	200	Skimmed milk	240
Bread			Whole wheat bread	20
Butter			Butter	5
Beverage	Tea with lemon	1 cup	Tea with lemon	1 cup

TABLE XIV

Sample Menu for Low Calorie Diets

	Special 1,200 calorie		1,500 calorie	
	Food	Weight, gm.	Food	Weight, gm.
Breakfast				
10% fruit	Grapefruit	100	Grapefruit	100
Egg	Egg, soft cooked	one	Egg, soft cooked	one
Bread, toasted	Whole wheat toast	20	Whole wheat toast	20
Butter	Butter	5	Butter	5
20% cream	Cream	30	Cream	30
Beverage	Coffee	1 cup	Coffee	1 cup
Dinner				
Soup	Broth	1 cup	Broth	1 cup
Lean meat	Lean roast beef	75		
Meat			Roast beef	75
20% vegetable			Mashed potato	100
3% vegetable	New cabbage	100	New cabbage	100
3% vegetable	Tomato salad	100	Tomato salad	100
10% fruit	Orange slices	100	Orange slices	100
Skimmed milk	Skimmed milk	240		
Whole milk			Whole milk	240
Bread			Whole wheat bread	20
Butter	Butter	5	Butter	10
Supper				
Lean meat	Lean cold ham	75		
Meat			Cold sliced ham	75
3% vegetable	Green beans	100	Green beans	100
3% vegetable	Celery and carrot sticks	50 25	Celery and carrot sticks	50 25
10% fruit	Water packed pears	100		
25% fruit			Canned pears	100
Skimmed milk	Skimmed milk	240		
Whole milk			Whole milk	240
Bread	Whole wheat bread	20	Whole wheat bread	20
Butter	Butter	5	Butter	10
Beverage	Tea with lemon	1 cup	Tea with lemon	1 cup
3 p m Skimmed milk	Skimmed milk	240		
8 p m Skimmed milk	Skimmed milk	240		

milk a day. It is suggested for children or pregnant requiring reduction of weight and could be used with fications in cases of obese patients with gastric or ulcer.

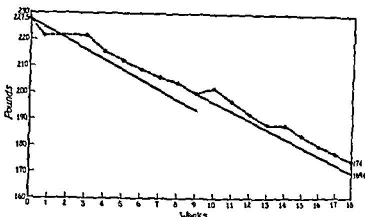


Figure 7: Calculation of predicted weight loss for a thirty two year old woman, 63.5 inches in height, weighing 227.5 pounds: basal calories for 195 pounds, 1,640; basal calories plus 50 per cent, 2,460; caloric intake, 620; caloric deficit, 1,840; predicted average weight loss, 3.7 pounds per week for the first nine weeks, or 33 pounds After nine weeks the patient weighed 200 pounds, the actual loss being 27.5 pounds.

Calculation of the predicted weight loss for the next nine weeks was as follows: basal calories for 170 pounds, 1,540; basal calories plus 50 per cent, 2,310; caloric intake, 620; caloric deficit, 1,690, predicted average weight loss per week, 3 4 pounds, or 31 pounds in the second nine weeks The actual loss in this second nine week period was 26 pounds Six months later this patient weighed 143 pounds (The solid line represents the predicted weight loss; the broken line, the actual weight loss.)

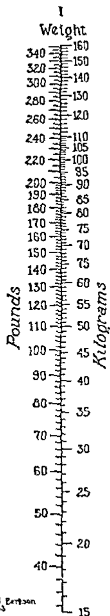
One multiple-vitamin capsule each day is routinely given to all patients on these diets Salt and water are not restricted. In hospitals using separated skimmed milk, the fat content of the 600 and 1,000 calorie diets will be even lower than indicated by about 4 gm. or 36 calories. *Vegetables* used may be either fresh, canned or frozen, but are limited either to those containing approximately 3 per cent of carbohydrate or to half the number of grams of those containing 6 per cent of carbohydrate, except in the 1,500 calorie diet, which allows 100 gm of a 20 per cent vegetable or a cooked

For your convenience, this may be removed by tearing on perforated line

Mayo Foundation Standards for age and sex

Food Nomogram

Directions The standards for age are arranged on the basis of the common method of expressing age as of the last birthday To determine the desired calorie allowance, proceed as follows (1) Locate the weight on Scale I by means of a pin stuck through the eraser of a lead pencil (2) Place the edge of the ruler against the pin and swing the other end of ruler to the patient's height on Scale II (3) Transfer the pin to the point where the ruler crosses Scale III which gives the surface area in sq meters (this value need not be read) (4) Holding the ruler against pin on the surface area scale, swing the left hand end of the ruler to the patient's standard for age and sex given on Scale IV (5) Transfer the pin to where the ruler now crosses Scale V which gives the basal heat production of the patient for 24 hours and represents the calories of food required by the fasting patient when resting in bed (basal calories) The calories necessary for activity bear a percentage relationship to those demanded for the resting condition The so-called "white collar worker" when at work will need about 50 per cent more than his basal calories When activity is restricted, as in the hospital, the extra calories necessary will range from 10 to 30 per cent of the basal calories Therefore (6) estimate the per cent of calories above the basal and locate this point on Scale VI With the ruler connect this point with the point located previously on Scale V, and where the ruler now crosses Scale VII read the amount of food calories to be provided by the diet

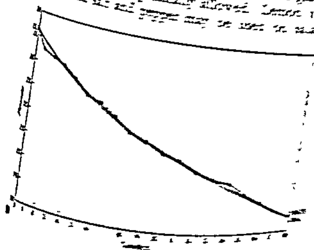


W M Boothby and J Berkson
October 1933

B. Saunders Company)

eal product, such as rice, macaroni or spaghetti once a day. Fruits must either be fresh or canned without sugar, except in the 1,500 calorie diet which includes one fruit per day, canned in light syrup. Water packed fruits canned without sugar are used almost exclusively in the very low calorie diets, since many contain only 5 per cent of carbohydrate. The meats used must be lean, free from visible fat and cooked without fat. Meat is weighed after cooking. Fish, chicken and liver may be used to advantage since they are very lean, these are calculated as containing 5 per cent of fat, although Strang and Evans did not consider the fat content of lean meat to be of any significance. No fats are allowed on the 600 calorie diet except those naturally found in protein foods.

Much of the variation found in the actual number of calories reported in low calorie diets is due to differences in values for per cent of fat in cooked lean meat used in the calculations. Fats are restricted on all low calorie diets because of their high caloric value per gram. Bacon, sausage, oil, bacon fat, chicken fat, vegetable fats, sauces and gravies must be avoided unless specifically allowed. Lemon juice or vinegar, and salt and pepper may be used to make



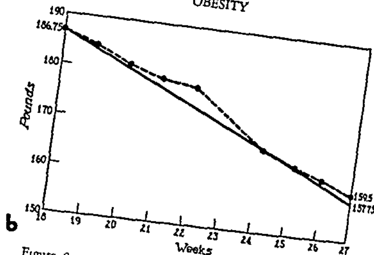


Figure 8a and 8b Calculation of predicted weight loss for a thirty-nine year old woman, 62 25 inches in height, weighing 252 5 pounds basal calories for 222.5 pounds, 1700; basal plus 50 per cent, 2,550, caloric intake, 620; caloric deficit, 1,930; predicted average weight loss, 3 9 pounds per week or 35 pounds in the first nine weeks After nine weeks she weighed 218 pounds, an actual loss of 34 5 pounds

Calculation of weight loss for the next nine weeks was as follows basal calories for 188 pounds, 1,580, basal plus 50 per cent, 2,370, caloric intake, 620, caloric deficit, 1,750; predicted average weight loss, 3 5 pounds per week or 31.5 pounds in the second nine weeks At the end of this period she weighed 186 5, an actual loss of 31 5 pounds

Calculation of weight loss for the third nine week period was as follows. basal calories for 155 pounds, 1,480, basal plus 50 per cent, 2,220; caloric intake, 620, caloric deficit, 1,600; predicted average weight loss per week, 3 2 pounds, or a loss of 29 pounds in the third nine week period At the end of this period she weighed 159.5 pounds, an actual loss of 27 pounds. Two months later she weighed 148 pounds, a total loss of 104 5 pounds. (The solid line represents the predicted weight loss, the broken line, the actual weight loss)

Spices are allowed but condiments containing sugar or fat, such as relishes, chili sauce, catsup, pickles and olives must not be used. Saccharin may be used as a sweetener in bev-

TABLE XV

SUBSTITUTIONS

	Gm
Substitutions for 100 gm. of 3 per cent vegetable	
1. 6 per cent vegetable	50
2. 5 per cent fruit	60
3 10 per cent fruit	30
4. 15 per cent fruit or vegetable	20
5. 20 per cent fruit or vegetable	15
Substitutions for 100 gm. of 10 per cent fruit	
1. 3 per cent vegetable	335
2. 6 per cent vegetable	165
3. 5 per cent fruit	200
4 15 per cent fruit or vegetable	65
5. 20 per cent fruit or vegetable	50
6. Dry cereal	13
7. Soda crackers	14
8. Bread	20
Substitutions for 20 gm. of bread	
1 3 per cent vegetable	335
2. 6 per cent vegetable	165
3. 5 per cent fruit	200
4 10 per cent fruit	100
5. 15 per cent fruit or vegetable	65
6 20 per cent fruit or vegetable	50
7. Dry cereal	13
8. Soda crackers	14
9. Flour	14
Substitutions for 240 gm of whole milk	
1. {10 per cent fruit	120
{Egg	1 egg
2. {Bread	25
{Meat, cooked	20
{Butter	10
Substitutions for 240 gm. of skimmed milk	
1. {10 per cent fruit	120
{Meat, very lean	25
2 {Bread	25
{Meat, very lean	25
3 Buttermilk	240

erages and fruits if desired. Clear tea, black coffee and fat-free broth or bouillon may be taken between meals to appease the appetite.

TABLE XVI

Food Values

[illegible] given in Table XV.

Fruits Classified by Carbohydrate Content

3 per cent	6 per cent	15 per cent	20 per cent
Asparagus	Beets	Artichokes	Corn
Beet greens	Carrots	Green peas	Hominy, cooked
Broccoli	Kohlrabi	Parsnips	Lima beans, canned
Brussels sprouts	Okra		Macaroni, cooked
Cabbage	Onions		Noodles, cooked
Cauliflower	Pumpkin		Potato
Celery	Rutabagas		Rice, cooked
Cucumbers	Hubbard or winter squash		Shelled beans, cooked
Dandelion greens	Turnips		Spaghetti, cooked
Eggplant			
Endive			
Green peppers			
Lettuce			
Mushrooms			
Radishes			
Sauerkraut			
Spinach			
String beans			
Summer squash			
Swiss chard			
Tomato			
Water cress			

Sample menus for one day for diets of various caloric levels are given in Tables XIII and XIV. Also groupings of vegetables and fruits, food composition tables and substitutions which are helpful to the average patient, may be found in Tables XV, XVI, XVII and XVIII.

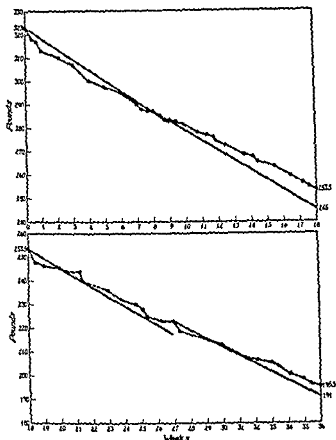


Figure 9: Calculation of predicted weight loss for a thirty-four year old woman, 63 5 inches in height, weighting 323 pounds basal calories for 293 pounds, 1,940, basal calories plus 50 per cent, 2,910, caloric intake, 620, caloric deficit, 2,290, predicted average weight loss, 4 6 pounds per week, or 41 pounds in the first nine week period. At the end of this period she weighed 283 pounds, an actual loss of 40 pounds

Calculation of the predicted weight loss for the second nine week period was as follows basal calories for 253 pounds, 1,810, basal calories plus 50 per cent, 2,715, caloric intake, 620; caloric

deficit, 2,095, predicted average weight loss, 4.2 pounds per week, or 38 pounds in the second nine week period. At the end of this period she weighed 253.5 pounds, an actual loss of 29.5 pounds

Calculation of the predicted weight loss for the third nine week period was as follows: basal calories for 223 pounds, 1,760, basal calories plus 50 per cent, 2,640, caloric intake, 620; caloric deficit, 2,020, predicted average weight loss, 4 pounds per week, or 36 pounds in the third nine week period. At the end of this period she weighed 224 pounds, an actual loss of 29.5 pounds

Calculation of the predicted weight loss for the fourth nine week period was as follows: basal calories for 190 pounds, 1,620; basal calories plus 50 per cent, 2,430; caloric intake, 620; caloric deficit, 1,810, predicted average weight loss, 3.6 pounds per week, or 32 pounds in the fourth nine week period At the end of this period she weighed 195.5 pounds, an actual loss of 28.5 pounds Eighteen weeks later she weighed 161 pounds, a total loss of 162 pounds in fifty-four weeks.

TABLE XVII

Fruits Classified by Carbohydrate Content

5 per cent	10 per cent	15 per cent	20 per cent
1. Fresh or juice packed			
Rhubarb	Blackberries Cantaloupe Cranberries Gooseberries Grapefruit Honeydew melon Lemons Limes Oranges Peaches Pineapple Strawberries Watermelon	Apples Apricots Blueberries Cherries Currants Huckleberries Pears Raspberries	Bananas Grapes Plums
2. Water packed			
Apricots Blackberries Cherries, red Cherries, white Loganberries Peaches Raspberries Strawberries	Applesauce Cherries, black Fruit for salad Pears Pineapple Plums White grapes	Kadota figs	

TABLE XVIII

Average Composition of Common Foods

	Per 100 gm. of food		
	Carbohydrate, gm.	Protein, gm	Fat, gm
Vegetables and fruits			
3 per cent vegetables	3	1	0
6 per cent vegetables	6	1	0
15 per cent vegetables	15	2	0
20 per cent vegetables			
Potato	20	2	0
Shelled beans	20	7	0
Green corn	20	3	1
5 per cent fruits	5	1	0
10 per cent fruits	10	1	0
15 per cent fruits	15	1	0
20 per cent fruits	20	2	0
Cereals and breadstuffs			
Breakfast cereals, dry	76	11	3
Breakfast cereals, cooked	11	1	
White bread	52	9	2
Whole wheat bread	48	10	4
Rye bread	52	6	3
Wheat flour	76	11	1
Soda crackers	73	10	11
Dairy products			
Whole milk	5	3	4
Skimmed milk	5	3	1*
Cream, light or coffee	4	3	20
Cream, heavy or whipping	4	3	30
Buttermilk	5	3	1*
Cheese, cheddar type	2	24	32
Cottage cheese, dry	4	20	1
Cottage cheese, creamed	4	20	5
Eggs, each		6	6
Meats and fish			
Meat, cooked, very lean		25	5
Meat, cooked		25	15
Meat, cooked, very fat		25	30
Fish, miscellaneous		20	3
Oysters	4	6	1
Liver	4	20	4
Cooked bacon		25	50
Fats			
Butter or oleomargarine			81
Lard or bacon fat			100
Olive oil and other oils			100
Mayonnaise	3	2	78
Peanut butter	21	26	48

* Fat negligible in commercially separated milk.

Chapter VI

OTHER THERAPY

PSYCHOTHERAPY

THE MOTIVES which take the obese to the doctor are many and the success of the treatment in the individual case depends in some measure on that motive.[409] Almost universally, patients in charity clinics have done poorly[70] unless they have shown some unusual desire to lose weight. If the patient comes only at the urging of someone else, it is unlikely that his determination will be sufficient to carry him through an adequate program of reduction It is the doctor's task to supply this determination by whatever means he can find Even more difficult is the problem of convincing the *obese patient who visits his doctor for some other complaint* of the necessity for reduction of weight. Better prospects face those patients who come voluntarily
impressed, by some dramatic incident
of cardiac decompensation or the onset
fact that obesity may cause harm

Under the term "psychotherapy"
pression which the personality and
make on the patient. Under this
all of those nebulous psychologic
doctor-patient relationship. The p
ner inspires confidence and a
most likely to be successful.

Ross[325] has shown quite we
completely convinced of the
will, by his manner, transmit
If there is a large psychologic
remarkable improvement foll

ther impressed by the worth of his therapy. A similar ph
nomenon may occur in the treatment of obesity. The docto
who believes he has found an endocrine or other preparatio
that will cure obesity will have the patient return to his
office at frequent intervals for injections. The patient, impressed by the doctor's enthusiasm for his drug, becomes hopeful for success and anxious to aid in every way possible. Under such circumstances it is not surprising that the dietary instructions are followed more closely so that a good result is obtained. Thus the physician is further convinced of the efficacy of his drug. It is only when the doubting physician uses the drug that it fails.

On the other hand, it may be difficult to maintain the faltering patient's morale without such a device. The patient may see little to be gained from periodic visits to the doctor's office if he receives no special treatment at these visits. For this reason, the interval between visits may lengthen, the patient's will to lose weight weakens and violations of the diet occur. McCullagh[240] has emphasized the importance of regular visits. The maintenance of the patient's determination to follow the diet and to lose weight is an important factor, and the success of the treatment may be determined by how well the physician is able to do this. Since each patient is different, the physician unconsciously adopts varying technics and approaches to such problems. Richardson[819, 820] expressed the belief that the success of a program of weight reduction depends largely on the patient's understanding of the psychologic factors involved and on the doctor's utilization of those factors.

Ordinarily the patient is not sufficiently impressed with the seriousness of his condition, so that it frequently becomes necessary for the physician to alarm the patient deliberately.

The patient can be told that "between the ages of 45 and 55, 25 pounds of excess weight means a 25% increase in the chances of your dying within the next year; 50 pounds excess means a 50% greater chance of death; more weight

increases the hazard in proportion."[284] Figure 1 illustrates this point, one can point to these mortality figures and accurately say to the patient, "You are digging your own grave with your teeth."

The patient should be told that his heart is working overtime to pump blood through the masses of fat, that his knees, hips and back are likely to become injured and painful because of long-continued obesity. The physician frequently will be able to tell the patient that "your heart is fine but the strain imposed on the heart by all this fat is just like the strain placed on an automobile motor by driving about with the brakes on. Although it may be a good motor, it's bound to wear out sooner if the brakes are kept on all the time."

For the person who still seems complacent, it may be necessary to compare them and their urge to eat with the alcoholic and his compulsion to drink. They can be told truthfully that the circumstances leading to gluttony and to alcoholism are much the same and that the results are about equally harmful.

The patient should be reassured that the reduction program will not harm him and that a familial tendency to or a long term duration of obesity is no bar to therapy. He should be told to disregard relatives and well-meaning friends who unconsciously associate loss of weight with ill health and tell him daily that "this diet makes you look terrible."

Superficial psychotherapy in the form of encouragement and reassurance may be sufficient in the majority of cases, but not infrequently greater benefit may result from more extensive investigation and treatment. Discussion of the patient's conflicts and problems and simple explanation of their origin, after the patient has spent several hours unburdening himself of them, can be given by the interested internist. It is only seldom that the internist will be forced to turn to the psychiatrist for help. Sometimes conflicts and

neuroses will be resolved by loss of weight so that systematic psychotherapy is not required. Schopbach and Matthews,[333] in one series of cases, found that the patients were unable to remain comfortable on their diets without psychiatric help.

There may be fears which the patient hesitates to express He may have some fear that he will become the victim of tuberculosis or some other wasting disease if he should become thin.[398] The pleasure of eating may have been a substitute for other pleasures of life which were denied the patient by circumstances or perhaps by his inability to experience pleasure. Many people, through early training, have become inhibited to such an extent that their acceptable pleasures are few, and eating is one of those which remains respectable. Still other people have a great deal of nervous tension and find that during periods of stress there is a compulsion to eat Such compulsive eating[84] is exemplified in the person who says "but I get so nervous I just have to eat something to quiet my nerves" Some people smoke, some drink, while others eat and get fat.

Even more important than the accomplishment of the initial loss of weight is the maintenance of the weight at a normal level. Unless some progress has been made in the solution of the patient's psychologic difficulties and unless some insight has been gained, it is unlikely that the normal weight, when reached, will be maintained in the person who became fat because of a neurosis[291] The establishment of new habits of eating, however, which is often accomplished by the reduction program, is sometimes all that is required for maintenance of normal weight.

DRUGS

Thyroid

This has been used since 1894 in the treatment of obesity.[419] It obtained early favor because obesity was, at that time, thought to stem frequently from hypothyroidism; therefore, it was felt that thyroid would act as a specific

remedy. However, as time proved that hypothyroidism was only occasionally associated with obesity, thyroid began to be used for its calorigenic action rather than as specific replacement therapy. Bram[40] has administered thyroid in amounts sufficient to cause basal metabolic rates of + 15 and + 20 with a pulse of 90 in a variety of conditions, including obesity. Winkler[417] expressed the belief that ordinary doses of thyroid administered to the individual with a normal thyroid are inactivated. Selye[336] pointed out that a gland is put at rest by the administration of the hormone specific for that gland, and Cramer[83] and Farquharson and Squires[128] advised that increasing doses of thyroid are required to maintain the basal metabolic rate. Soskin and Levine[354] stated that the administration of thyroid inhibits the formation of thyrotropic hormone by the pituitary.

Although it has been adequately demonstrated that basal metabolic rates which are computed on the basis of surface area are essentially normal in obesity, studies related to the effect of low calorie diets on the basal metabolic rate in the obese are few. It is felt by some that the basal metabolic rate drops to less than normal during the process of reduction[25, 56, 88, 234, 261, 368] and that thyroid should be given in order to maintain metabolism at a normal rate.[88, 116, 155, 233] Others have calculated that the energy output of the obese person is dangerously high, when computed on the basis of ideal weight,[110, 125, 127] and have failed to find more than occasional falls in the basal metabolic rate as the result of restriction of diet.[131, 257, 268, 275] Wilder[408] has stated that an adequate dietary supply of protein prevents this fall in basal metabolic rate

The heart, lungs, muscles and liver of the obese are under increased strain because of the obesity. As was mentioned in the section on physiology, since the obese person has a dangerously high rate of metabolism although when computed on the basis of surface area it seems normal, it is easy to see how thyroid might easily cause undesirable and

excessive strains on the circulatory system of an obese person if the basal metabolic rate were even moderately elevated by administration of this substance In addition, the harmful effects of thyroid on the heart are not limited to the extra work occasioned by the elevation of the basal metabolic rate, but they also depend on a direct toxic action.[313] These facts, however, should not prevent the use of thyroid in the treatment of obesity in the person with hypothyroidism, provided periodic determinations of the basal metabolic rate are made as a guide to therapy

It is felt by some that thyroid may be effective in doses too small to yield any calorigenic action.[167] This is supposed to depend partly on a diuretic action of thyroid,[167, 297] but otherwise the mechanism is obscure. It is known that thyroidectomy tends to cancel the diuresis of diabetes insipidus,[83] but whether thyroid has a direct diuretic effect in the person with normal pituitary function has not been so well demonstrated, although the latter has been implied[220] Administration of thyroid was found by Plummer[302] to cause the loss of an average of thirteen pounds (5 9 kg) of fluid from the tissues of the myxedematous patient, but convincing proof of such an action in the euthyroid individual is lacking

Means[261] and Sevringhaus,[338, 339] on the other hand, agreed that thyroid is effective only by causing hyperthyroidism and that it should not be used in obesity except in very special situations Barborka[12, 13] and Bulger[73] cautioned against the indiscriminate use of thyroid

Lyon and Dunlop[235] suggested that thyroid may produce loss of weight partly by destruction of protein, that is, by causing a negative nitrogen balance, and by diuresis It is known that a considerably larger amount of water is associated with protein in the body than with fat, and if there is loss of isocaloric quantities of tissue protein and fat, there is a much greater (approximately ninefold) loss of weight because of the destruction of protein[290] Mason noted con-

siderable losses of nitrogen when obese patients were given thyroid and diets containing 24 gm. of protein.[242] Studies by Boothby and co-workers[38] demonstrated that a negative nitrogen balance follows administration of thyroxin Others[48, 61] simply found that thyroid is ineffective in causing reduction of weight. Fellows[131] found thyroid effective in a few patients with persistently low basal metabolic rate and obesity, but only as an adjuvant to diet.

Bram has reported five cases of exophthalmic goiter following therapy with thyroid,[40] and exophthalmos alone following such therapy has been described.[23] Thyroid with minute amounts of bromide in chemical combination has been considered by some investigators to have fewer "toxic effects" for the same metabolic action[130] than does thyroid alone. It is questionable, however, whether any preparation of thyroid can be said to have fewer "toxic effects," sinc these symptoms seem to arise from the thyroxin molecul itself and are bound up closely with the desirable therapeut effects.

It is probably wise in many cases to determine the bas metabolic rate prior to starting any reduction therapy in t obese, if only to be able to tell the patient, with convicti that "your thyroid gland is functioning normally and important thing is diet and not the use of thyroid." results of determinations of basal metabolic rates in o children may be unreliable.

In summary, the obese person is unusually susceptib harm from administration of thyroid because of his al elevated rate of metabolism Thyroid given in small do probably inactivated and is, therefore, likely to be ineffe Thyroid administered in larger doses may cause a re of weight through destruction of tissue proteins and l vation of the basal metabolic rate, but its harmful eff the circulatory system make it a dangerous agent. If thyroidism is associated with the obesity, enough in ment in subjective symptoms and mood may resu

therapy with thyroid, so that proper diet, the mainstay of reduction therapy, may be adhered to with greater ease.

Other endocrine preparations

Other endocrine preparations have been used to cause reduction of weight,[124, 149] and some authors have expressed the belief that there are cases in which reduction by diet alone is impossible and that endocrine therapy is essential

Extracts of the anterior lobe of the pituitary gland have been tried;[36, 48, 141, 208] it is significant that the same extracts have been recommended for both the cachexia and the obesity that are supposed to follow pituitary disease[65, 74]

Estrogens have been used[149, 151] but there is no adequate proof that a deficiency of them causes obesity In addition, estrogens tend to cause retention of water and, hence, a temporary gain in weight. Therefore, their use cannot be advised for the treatment of obesity itself.

Testosterone causes an increase in the amount of muscular tissue and a change in the pattern of distribution of fat in the male with hypogonadism, but such cases of hypogonadism are not frequent. It is unlikely that any benefit will follow the use of testosterone in obesity, although such use has been suggesetd[383]

Werner[400] has used obstetric pituitrin in conjunction with thyroid. A possible basis for this view might be found in experiments which were thought to demonstrate the occurrence of both obesity and diabetes insipidus after injury to the posterior lobe[203, 204] of the pituitary gland, but no adequate proof of the effectiveness of pituitrin has been advanced.

Ovarian extracts[208] and chorionic gonadotropin[48, 151, 383] have been used but without convincing results.

Amphetamine

Various sympathomimetic amines have been used both as metabolic stimulants and as appetite depressors. The most

extensively used among these drugs is amphetamine sulfate (benzedrine sulfate).[170, 217, 298, 299] One of the earliest studies on the use of benzedrine in obesity was performed by Lesses and Myerson[226] in 1938. They expressed the belief that the normal appetite mechanism will adjust the intake of energy to meet the requirements of expenditure of energy and, thereby, will cause maintenance of constant weight They pointed out that social and economic environments make food available with little exertion to many and that a symptom complex which they have named "anhedonia" is frequently seen[277] In this condition there is a diminution in the pleasure ordinarily derived from life's activities. When enjoyment from other activities is impaired, then the person turns to eating only to find that more and more food is required to give satisfaction. They expressed the belief that most of the food eaten by the person with anhedonia is characteristically consumed during the second half of the day Such patients, Lesses and Myerson considered, can be best treated with benzedrine, which is thought to have a direct depressing action on appetite and to cause increased activity They did not restrict use of this drug to the variety of obesity seen in anhedonia, and they obtained good results in all persons receiving it. Placebos failed to help control patients They found no tolerance toward this drug developed as far as the appetite was concerned. Others have observed such a tolerance, however.[48, 376]

Earlier, Myerson, Loman and Dameshek[278] studied benzedrine and cautioned against the use of this drug in the presence of hypertension, particularly if it is to be used in conjunction with atropine, since the synergistic action of the two drugs makes pressor response maximal. Results of laboratory studies suggest, however, that a tolerance to the pressor effects of many sympathomimetic drugs, including benzedrine, is rapidly acquired.[293]

Rosenthal and Solomon[324] expressed the belief that they obtained loss of weight from use of benzedrine without re-

striction of diet, although they stated that the drug may be of greatest aid by helping the patient to stay on a diet as a result of improvement of mood. No increase in basal metabolic rate[324] was found, although there appeared to be an increase in the output of energy as a result of increased activity. These authors also expressed the belief that benzedrine acts as a diuretic. Ersner[123] found no elevation of the basal metabolic rate and observed that the blood pressure fell in association with benzedrine-induced loss of weight. Beyer,[29] in carefully controlled experimental work, found a 15 per cent increase in the basal metabolic rate, which lasted nine to twenty-four hours, and a considerable increase in blood pressure after 30 mg doses of benzedrine had been administered orally. Emerson[119, 120] has carried out determinations of basal metabolic rate during a three hour period which followed the ingestion of 20 mg doses of amphetamine by human subjects. He found that the racemic form caused a maximal rise of 15.7 per cent, the levorotatory isomer, a rise of 5.5 per cent, and the dextrorotatory isomer, a rise of 11.5 per cent in the basal metabolic rate. Thus it seems likely that ingestion of amphetamine will cause some elevation in the basal metabolic rate, according to the results of determinations made within several hours, but if there has been no medication for twelve to eighteen hours, little or no effect will be observed.[219]

Kunstadter and Necheles[218] found, after administration of benzedrine, diminished gastric motility which they considered to be the mechanism of appetite depression.

A convincing study on both dogs and human subjects was carried out by Harris and Ivy.[168, 169] They found that a definite loss of weight took place during therapy with racemic or dextrorotatory amphetamine which was the result of voluntary reduction in intake of food. No diuresis or increase in basal metabolic rate was noted, but the occurrence of a slightly greater than expected loss of weight suggested that there might be some increase in total metabolism the

first few days after administration of the drug had been started. Anorexia was proved, by experiments on dogs on which vagotomy and splanchnolumbar sympathectomy had been performed, to be central in origin and to be independent of any effects of amphetamine on gastric motility or secretion. Appetite returned to normal quickly after administration of the drug had been stopped. Sufficiently large doses of amphetamine prevented dogs from eating for as long as twenty-one days. The average dose employed in human subjects by these experiments was 5 mg. of dextrorotatory amphetamine or 10 mg. of the racemic form three times daily.

Maclagen,[246] in well-controlled animal experiments, could demonstrate no effect of ephedrine or benzedrine on appetite, although pitressin and atropine in large doses had some diminishing effect.

Cutting[88] found little help from use of amphetamine, propadrine or belladonna in programs of weight reduction Bruch[71] found that the results of benzedrine therapy were equivocal and stated that perhaps some of the apparent benefit may result from the increased enthusiasm of the patient for the entire program if he is receiving a drug which he thinks is specific She noted that often an obese patient will ask for the renewal of some prescription given for some incidental reason because he feels that it has helped him to follow his diet Kalb[198, 199] has found that administration of neither amphetamine nor thyroid increases the rate of loss of weight that is obtained by use of a submaintenance diet alone.

More recently, studies have differentiated the effects of the two optical isomers of benzedrine. Prinzmetal and Alles[5, 305] found that although the dextrorotatory, levorotatory and racemic forms had equal pressor effects, the dextrorotatory isomer had three to four times the stimulating effects on the central nervous system that the levorotatory form possessed. Other studies have confirmed this greater

central activity of the dextrorotatory form in connection with a variety of sympathomimetic amines Schulte and co-workers[335] found that the major portion of the stimulating activity of racemic amphetamine on the central nervous system resides in the dextrorotatory isomer, and of a number of sympathomimetic amines, dextrorotatory amphetamine was by far the most potent.

The opinion has been expressed that the "undesirable excitatory effects" of benzedrine reside chiefly in the levorotatory form,[80] while the desirable appetite-depressing effects, which also presumably result from stimulation of the central nervous system, are a property of the dextrorotatory form. This group of clinical investigators found dextrorotatory amphetamine, racemic amphetamine, propadrine, and levorotatory amphetamine to be decreasingly effective in the order listed. They also used thyroid, ammonium chloride, mercurial diuretics and decholin in varying succession as a means of preventing the patient from becoming discouraged[80]

Dextrorotatory desoxyephedrine has also been used[137] but this substance is considered more likely to produce undesirable effects, such as emotional irritability, than does amphetamine.[93] Albrecht[2] found that the increase in blood pressure which follows benzedrine therapy persists only a few days but expressed the belief that the drug should be used carefully or not at all in coronary artery disease, excitability, insomnia or hypersensitivity to epinephrine-like compounds Swanson and others[373] showed that the levorotatory isomers of a number of sympathomimetic amines always had a greater pressor activity than the dextrorotatory forms

Hirsh[179] considered propadrine to be the best of this group of drugs with which to control appetite

Freed[137] has found that no increase in blood pressure results from administration of benzedrine and expressed the belief that its use is unnecessary after about two months,

since by that time the appetite seems permanently depressed.

The Council on Pharmacy and Chemistry of the American Medical Association[358, 359] in 1943 condemned the use of benzedrine in the treatment of obesity because "whatever effectiveness the drug might possess might possibly be due to undesirable properties." More recently, however, the Council has accepted the use of amphetamine, with this statement: "In the light of recently developed evidence the Council now believes that amphetamine sulfate may be used in the management of obesity provided the dosage is held by the physician within such limits as may be necessary to produce the desired effect of reduction of appetite in the individual. This, of course, does not contemplate the indiscriminate use of the drug, either by prescription or over the counter sale."[7] The Council has particularly censured the use of benzedrine in complex mixtures of laxatives, atropine and sedatives.[6, 358, 359] A system of treatment in which varicolored pills composed of such mixtures are used has been called, popularly, the "technicolor method" of weight reduction.

Addiction[353] and psychotic symptoms[293] associated with benzedrine therapy have been reported but seem to be rare. Suicide[142] caused by the ingestion of benzedrine has been reported

In summary, the final estimation of the usefulness and dangers of amphetamine and allied drugs is yet to be made. The bulk of evidence suggests, however, that these drugs do produce a true anorexia and that, under ordinary circumstances and in moderate doses, they apparently cause little adverse effect on the cardiovascular system. The indiscriminate use of drugs of this group is to be deplored; particularly undesirable is the use of them in complex mixtures of other drugs A rise in blood pressure, psychologic dependence on the drug, undue stimulation and sleeplessness, and nervousness are indications for stopping use of the drug. Although statements are frequently made that the blood

pressure and the basal metabolic rate are not affected by amphetamine, it seems likely that adequate measurements made in the few hours after administration of the drug will detect appreciable and sometimes dangerous elevations in both. It must be remembered that careful instructions in diet are important whether or not amphetamine is used, in order that the diet which is limited in calories will not be deficient in essential food elements.

Dinitrophenol

This is another drug which presents the advantages of a convenient pill and which promises the patient effortless reduction of weight. However, the frequent occurrence of skin rashes, neuritis, agranulocytosis and cataracts makes it an undesirable drug, so that now it is never used.[225, 355, 377] This drug acts by causing increase in the basal metabolic rate and, thereby, consumption of the excess tissue When diet is not restricted, dinitrophenol is of little benefit[18, 353]

Belladonna

This drug has been used with some apparent success to diminish the appetite.[137, 246, 293] The mechanism suggested is that gastro-intestinal motility is diminished. No conclusive studies have been carried out with this drug, however, and it seems to have no specific effect on the appetite unless it is used in large amounts[246]

Miscellaneous therapy

Miscellaneous therapy, none of which has been widely used, is mentioned only for the sake of completeness Seaweed, iodine and barium compounds have been tried[152] Digitalis[41, 42, 44] and bulk-producing laxatives[292] have been proposed as devices to lessen appetite. Nonspecific protein therapy[294] and ultraviolet irradiation[208] have been urged On the border of quackery is the use of soaps, bath salts and mechanical machines for reduction of weight[409] Emetics

and high colonic irrigations are ineffective and unwise.[409]

The use of candy in small amounts preceding each meal has been suggested as a means of "killing the appetite," but the effectiveness of this practice is to be questioned.[44, 150] It has been suggested that glucose eaten between meals is "consumed as fuel" and is not deposited as fat,[150] but this opinion is also to be doubted.

Diuretics

Use of diuretics may give the physician and the patient a false sense of achievement by causing the excretion of a few pounds of water. Mason and Hellbaum[251] demonstrated that the ingestion of 36 gm. of sodium bicarbonate in three days by medical students caused an average gain of 2.28 pounds (1.03 kg.) while ingestion of 18 gm. of ammonium chloride in a period of similar length caused an average loss of 1.97 pounds (0.89 kg.). Occasionally the physician may find it necessary to encourage the faint-hearted patient by means of diuretics which cause the rapid excretion of a few pounds of water, but this should be considered only as a means of psychotherapy and not as a specific device for the correction of obesity. The success of a program for reduction of weight should not be judged by the day-to-day loss of weight, since variations in the amount of water ingested may amount to three or four pounds (1.4 to 1.8 kg.) daily so that such variations are of little significance in the final result of therapy.

Diuretics have the fault common to all medications in that they also divert the patient's attention from the principal therapeutic device of diet, so that he is thereby tempted to eat as his appetite demands and rely on the needle or pill to cause reduction.

Many capable workers have used diuretics, however.[158, 170, 299] Pelner[299] expressed the belief that there is significant retention of water in every obese patient and that most patients will require diuretics.

Urea has been suggested as a diuretic.[158] If diuretics are to be used it is suggested that the less harmful ones, such as ammonium chloride and urea, be employed.

HEAT CABINET TREATMENTS (TURKISH BATHS) AND SALT RESTRICTION

Treatment in heat cabinets causes the loss of water and electrolytes as a result of increased perspiration, so that any loss of weight obtained by this means is temporary and limited in amount.[386]

The restriction of salt in the diet[275, 299] aids in the loss of weight in the same manner as does the administration of diuretics and Turkish baths. Sodium is the "backbone" of the extracellular fluid;[140] an excess of sodium encourages retention of water, but a scanty supply encourages the excretion of water.

The restriction of water which is sometimes advised[151] serves no useful purpose.[387] The starving person usually tends to consume an excess of water, perhaps in an attempt to assuage his hunger.[210] This is rapidly excreted so that, unless the intake of salt is increased or unless "starvation edema" occurs, there is no gain in weight "Starvation edema" is not known to occur in the obese person but it is often observed when the weight has diminished to a value well below normal as a result of starvation.

Zondek[423] expressed the belief that obesity due to retention of water and salt is a frequent occurrence in the Middle East and that it does not respond to endocrine, dietary or psychologic therapy He regards restriction of water and salt and the use of mercurial diuretics as the crucial therapeutic measures in these cases. We have observed no such patients in the United States.

EXERCISE AND MASSAGE

These offer two popular but relatively ineffective methods of weight reduction.[348] Newburgh[285] estimated that the

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EXERCISE AND MASSAGE

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energy consumed in walking a mile equals 100 calories and that one must walk thirty-six miles (57.9 km) to lose one pound (0.5 kg.) of adipose tissue. Because exercise tends to increase appetite, it is very questionable whether vigorous exercise is of real aid in a program of reduction,[102] although hard physical labor may cause consumption of as much as 2,000 calories or more a day in excess of basal requirements

One should remember that the cardiovascular and respiratory organs in an obese person are already laboring under the strain of increased metabolism and that vigorous exercise will impose on them an even greater demand. A moderate amount of light exercise is to be encouraged during a period of reduction but such exercise should not be expected to increase significantly the rate at which weight is lost. Douthwaite[102] described exercises for strengthening the abdominal muscles and aiding posture which can be carried out by the patient while he is performing everyday tasks.

One of the common misconceptions concerning the treatment of obesity is that certain exercises or localized massage will remove fat selectively from specified sites.[223] Muscles can, of course, be developed selectively, and perhaps by this means some change in contour can be achieved. It has been fairly well demonstrated that vigorous massage will neither diminish the size of one limb compared to the corresponding member[200] nor mobilize enough fat to increase appreciably the concentration of blood lipoids.[348] Some evidence that massage will diminish the fat in the "fat organs" of rats was advanced by Tuerkisher and Wertheimer,[385] however.

Cold baths have been suggested as a means of increasing the output of energy, but the increase accomplished by this means is probably small.[394]

SURGICAL REMOVAL OF FAT

Procedures in which large masses of fat are surgically removed have been used but infrequently. Healing is often

delayed, sometimes it is never completed and there is always the danger of fat embolism. Plastic correction of large folds of skin which are left after extensive loss of weight may occasionally be necessary [195, 344]

REFERENCES

1. Ackerknecht, E. H.: The history of metabolic diseases *Ciba Symposia* 6:1838-1844 (June-July) 1944
2. Albrecht, F. K.: The use of benzedrine sulfate in obesity. *Ann. Int. Med.* 21:983-989 (Dec.) 1944.
3. Albright, Fuller: Cushing's syndrome; its pathological physiology, its relationship to the adreno-genital syndrome, and its connection with the problem of the reaction of the body to injurious agents ("alarm reaction" of Selye). *Harvey Lect.* 38·123-186, 1942-1943.
4. Alexander, Franz and Portis, S. A : A psychosomatic study of hypoglycaemic fatigue. *Psychosom. Med.* 6.191-206 (July) 1944.
5. Alles, G. A : Comparative actions of optically isomeric phenisopropylamines. *J. Pharmacol. & Exper Therap.* 66:1 (May) 1939.
6. American Medical Association Council on Pharmacy and Chemistry· *New and nonofficial remedies*, Chicago, American Medical Association, 1946, 653 pp.
7. American Medical Association Council on Pharmacy and Chemistry. *Personal communication to the authors.*
8. Anderson, A B · Loss of weight in obese patients on sub maintenance diets and the effect of variation in the ratio of carbohydrate to fat in the diet *Quart. J. Med* 13.27-36 (Jan.) 1944.
9. Angel, J. L , Paschkis, K , Matthews, R. A., Schopbach, R , and Swenson, P. C : Constitutional obesity *Am. J. Phys. Anthropol.* 4·257 (June) 1946.
10. Aschner, Bernhard· Über die Funktion der Hypophyse. *Arch. f. d. ges Physiol* 146:1-146 (June) 1912.
11. Barborka, C J : Obesity and its treatment. *Proc. Staff Meet, Mayo Clinic* 6·128-130 (Mar. 4) 1931.
12. Barborka, C. J : Obesity. *M. Clin. North America.* 21:23-39 (Jan) 1937
13. Barborka, C. J : Obesity in adults. *Proc. Inter-State Postgrad. M A. North America* (1944) pp. 240-244, 1945.
14. Barker, L F.: The obesities—their origins and some of the methods of reducing them. *California & West. Med* 37: 73-81 (Aug) 1932.

15. Barker, N W, Nygaard, K K, Walters, Waltman an Priestley, J T.: A statistical study of postoperative venou thrombosis and pulmonary embolism II Predisposing fac tors *Proc. Staff Meet., Mayo Clinic* 16.1-5 (Jan 2) 1941
16 Barnes, Broda O, and Keeton, R W · Experimental obesity *Am. J Physiol* 129 P305-P306, 1940
17 Bauer, Julius Obesity, its pathogenesis, etiology and treatment. *Arch. Int. Med* 67 968-994 (May) 1941
18 Bayer, Leona M, and Gray, H · Obesity treatment by diet, thyroid and dinitrophenol, result on 106 outpatients *Am J. M. Sc.* 189 86-91 (Jan) 1935
19 Beardwood, J T, Jr.: *The cyclopedia of medicine, surgery and specialties. Vol 10*, Philadelphia, F A Davis Company, 1945, pp 706-739
20 Beck, H G Dystrophia adiposogenitalis (Fröhlich's syndrome) In *Association for Research in Nervous and Mental Disease* The pituitary gland, an investigation of the most recent advances Baltimore, The Williams & Wilkins Company, 1938, pp 634-650
21 Beeler, Carol and Fitz, Reginald Observations on glycemia, glycuresis and water excretion in obesity *Arch Int Med* 28 804-812 (Dec) 1921
22 Behnke, A. R, Jr, Feen, B G, and Welham, W C The specific gravity of healthy men, body weight — volume as an index of obesity *J A M A* 118 495-498 (Feb 14) 1942
23 Behrman, Simon· Exophthalmos following abrupt discontinuation of thyroid medication for obesity *Proc Roy Soc Med* 38 665 (Oct) 1945
24 Benedict, F G, and Carpenter, T M *Food ingestion and energy transformations with special reference to the stimulating effect of nutrients.* Washington, D C, Carnegie Institution of Washington, 1918, 355 pp
25 Benedict, F G, Miles, W R, Roth, Paul, and Smith, H M *Human vitality and efficiency under prolonged restricted diet* Washington, D C, Carnegie Institution of Washington, 1919, 701 pp
26 Bergman, V.: Das Problem der Herabsetzung des Umsatzes bei der Fettsucht *Deutsche med Wchnschr* 1 611-613 (Apr. 8) 1909.
27 Bernhard, Karl, and Schoenheimer, Rudolf The rate of for-

mation of stearic and palmitic acids in normal mice. *J. Biol. Chem* 133:713-720 (May) 1940.

28 Bernhardt, Hermann: *New concepts concerning the pathogenesis of obesity and the problems of basal metabolism Endocrinology.* 14:209-225 (July-Aug.) 1930.

29. Beyer, K H: The effect of benzedrine sulfate (betaphenylisopropylamine) on metabolism and the cardiovascular system in man. *J. Pharmacol. & Exper. Therap. 66:318-325* (July) 1939.

30 Beznák, A. B L, and Hasch, Z.: The effect of sympathectomy on the fatty deposit in connective tissue. *Quart. J. Exper. Physiol.* 27:1-15, 1937.

31. Bing, J. F, Globus, J. H, and Simon, Helmuth: Pubertas praecox. a survey of the reported cases and verified anatomical findings, with particular reference to tumors of the pineal body. *J. Mt. Sinai Hosp. 4.935-965 (Mar.-Apr.)* 1938

32 Block, Malcolm. Rôle of lipophilia in the etiology of obesity *Proc. Soc. Exper. Biol. & Med. 49:496-499 (Mar.) 1942.*

33 Blotner, Harry, and Cutler, E. C.: Total thyroidectomy in the treatment of diabetes insipidus *J.A M.A.* 116.2739-2745 (June 21) 1941.

34. Bockus, H L. *Gastro-enterology; small and large intestine and peritoneum.* Philadelphia, W B. Saunders Company, 1946, vol 2, 975 pp.

35 Bollman, J L: Some experimental observations pertinent to the treatment of hepatic disease. *Ann. Int. Med* 12:1-5 (July) 1938

36. Bonime, R G. Obese thyropituitary deficiency in the female. *M. Clin. North America.* 30.683-706 (May) 1946

37. Boothby, W. M., and Sandiford, Irene: Summary of the basal metabolism data on 8,614 subjects with especial reference to the normal standards for the estimation of the basal metabolic rate *J. Biol. Chem* 54:783-803 (Dec.) 1922.

38. Boothby, W M, Sandiford, Irene, Sandiford, Kathleen, and Slosse, Jean. *The effect of thyroxin on the respiratory and nitrogenous metabolism of normal and myxedematous subjects. I A method of studying the reserve or deposit protein with a preliminary report of the results obtained Tr. A Am Physicians.* 40.195-229, 1925

39 Bowen, B D., Griffith, F. R., Jr, and Sly, Grace E.: The

effect of a high fat meal on the respiratory quotient and heat production of normal and obese individuals *J Nutrition* 8·421-434 (Oct.) 1934

40. Bram, Israel: Therapeutic hyperthyroidism *Internat Clin* 1:48 61 (Mar) 1937.

41 Bram, Israel. Digitalis in the dietary treatment of obesity, report of one hundred and forty cases. *M. Rec* 151 131-132 (Feb. 21) 1940.

42. Bram, Israel: The fat youngster, guiding principles in treatment of 200 cases of alimentary obesity in patients under age 15. *Arch. Pediat.* 60:239-249 (May) 1943

43 Bram, Israel: Psychosomatic obesity; with comments on 924 cases *M. Rec.* 157 673-676 (Nov) 1944

44 Bram, Israel. Appetite, hunger and obesity in youngsters past age twelve; deductions derived from over 1,000 cases *Arch. Pediat.* 63·581-585 (Nov) 1946

45. Brobeck, J. R: Mechanism of the development of obesity in animals with hypothalamic lesions. *Physiol. Rev* 26 541-559 (Oct.) 1946

46. Brobeck, J. R, Tepperman, Jay, and Long, C N H Experimental hypothalamic hyperphagia in the albino rat *Yale J Biol & Med.* 15:831-853 (July) 1943.

47. Brobeck, J R, Wheatland, Mary, and Strominger, J L Variations in regulation of energy exchange associated with estrus, diestrus, and pseudopregnancy in rats *Endocrinology* 40 65-73 (Feb.) 1947.

48 Bronstein, I P, Halpern, L J, and Brown, A. W Obesity in children *J. Pediat* 21 485-496 (Oct.) 1942

49. Brooks, C McC: Activity and the development of obesity *Federation Proc.* 5 (part 2)·12 (Feb) 1946

50 Brooks, C. McC.: The relative importance of changes in activity in the development of experimentally produced obesity in the rat *Am. J. Physiol.* 147 708-716 (Dec) 1946

51. Brooks, C. McC: A study of the respiratory quotient in experimental hypothalamic obesity. *Am. J Physiol.* 147·727-734 (Dec.) 1946.

52 Brooks, C. McC., and Bridge, E M: Changes in the respiratory quotient associated with development of experimentally produced obesity in the monkey (Macaca mulatta) *Endocrinology.* 35·208 (Sept) 1944

53 Brooks, C McC, and Lambert, E F. A study of the effect of limitation of food intake and the method of feeding on

the rate of weight gain during hypothalamic obesity in the albino rat. *Am. J. Physiol.* 147:695-707 (Dec.) 1946

54. Brooks, C. McC., and Marine, D. N.: A study of oxygen consumption in obesity. *Federation Proc.* 5 (part 2).12 (Feb) 1946

55 Brooks, C McC., Lambert, E. F., and Bard, Phillip: Experimental production of obesity in the monkey (Macaca mulatta). *Federation Proc.* 1:11 (Apr.) 1942.

56 Brooks, C McC., Lockwood, R. A, and Wiggins, M L: A study of the effect of hypothalamic lesions on the eating habits of the albino rat. *Am. J. Physiol* 147:735-741 (Dec.) 1946

57. Brooks, C McC, Marine, D. N, and Lambert, E. F.: A study of the food-feces ratios and of the oxygen consumption of albino rats during various phases of experimentally-produced obesity. *Am. J. Physiol.* 147:717-726 (Dec) 1946.

58 Brown, Edna G. and Ohlson, Margaret A: Weight reduction of obese women of college age; I. Clinical results and basal metabolism *J. Am. Dietet. A* 22.849-857 (Oct.) 1946

59 Brown, Edna G., Herman, Charlotte, and Ohlson, Margaret A Weight reduction of obese women of college age; II. Nitrogen, calcium, and phosphorus retentions of young women during weight reduction *J. Am. Dietet A* 22·858-863 (Oct) 1946.

60 Bruch, Hilde: Obesity in childhood I. Physical growth and development of obese children. *Am. J. Dis. Child.* 58·457-484 (Sept.) 1939.

61 Bruch, Hilde. Obesity in childhood II. Basal metabolism and serum cholesterol of obese children. *Am J. Dis. Child.* 58·1001-1022 (Nov.) 1939

62 Bruch, Hilde: The Fröhlich syndrome; report of the original case *Am. J. Dis Child.* 58:1282-1289 (Dec.) 1939

63 Bruch, Hilde: Obesity in childhood III. Physiologic and psychologic aspects of the food intake of obese children *Am. J. Dis Child* 59.739-781 (Apr) 1940.

64 Bruch, Hilde. Obesity in childhood IV. Energy expenditure of obese children. *Am. J Dis Child.* 60 1082-1109 (Nov) 1940

65 Bruch, Hilde· Obesity in childhood and endocrine treatment *J Pediat.* 18:36-56 (Jan.) 1941.

66 Bruch, Hilde: Obesity in relation to puberty *J Pediat.* 19. 365-375 (Sept) 1941

67. Bruch, Hilde· The grid for evaluating physical fitness (Wetzel); application to children with abnormal bodily dimensions. *J.A M.A* 118·1289-1293 (Apr. 11) 1942

68 Bruch, Hilde: Psychiatric aspects of obesity in children. *Am J Psychiat.* 99:752-757 (Mar) 1943

69 Bruch, Hilde· Dietary treatment of obesity in childhood. *J. Am Dietet. A.* 20.361-364 (June) 1944

70 Bruch, Hilde, and Touraine, Grace Obesity in childhood V. The family frame of obese children *Psychosom Med* 2·141-206 (Apr.) 1940

71 Bruch, Hilde, and Waters, Irene: Benzedrine sulfate (amphetamine) in the treatment of obese children and adolescents *J. Pediat.* 20.54-64 (Jan) 1942

72 Bulatao, E , and Carlson, A J. Contributions to the physiology of the stomach, influence of experimental changes in the blood sugar level on gastric hunger contractions *Am. J. Physiol* 69·107-115 (June) 1924

73 Bulger, H A.: Endocrine obesity *M Clin. North America* 20·369-378 (Sept) 1936

74 Calder, R. M. Pituitary cachexia (Simmonds' disease) treated with anterior pituitary extract *J A M A* 98.314-315 (Jan 23) 1932.

75. Campbell, W. R , and Maltby, E. J.: On the significance of respiratory quotients after the administration of certain carbohydrates *J. Clin Investigation* 6 303-317 (Oct) 1928

76 Cannon, W B., and Washburn, A. L · An explanation of hunger. *Am. J Physiol.* 29·441-454 (Mar 1) 1912

77 Carroll, H. H , and Russell, T. B . Glycosuria with diabetic type of glucose tolerance curves in obese nondiabetics *U. S. Nav. M Bull* 42.132-135 (Jan.) 1944

78. Cecil, R L.: *A textbook of medicine by American authors Ed 6*, Philadelphia, W B. Saunders Company, 1943, p 1312

79 Cheney, Garnett. Hunger and appetite, present conceptions in regard thereto *California & West Med* 30·145-150 (Mar) 1929

80. Colton, N. H , Segal, H I , Steinberg, A , Shechter, F. R , and Pastor, N.· The management of obesity with emphasis

on appetite control *Am. J. M. Sc.* 206:75-86 (July) 1943.

81. Conn, J W.: Obesity. II. Etiology aspects *Physiol Rev.* 24.31-45 (Jan.) 1944.
82. Coombs, H. I.: Obesity: its classification and causation *Brit. M. J.* 2:346-348 (Aug. 15) 1936
83 Cramer, H. I.: Physiological considerations of the etiology and treatment of obesity. *Canad. M.A.J.* 55:505-510 (Nov) 1946.
84. Crider, Blake: Psychotherapy in a case of obesity. *J. Clin. Psychol.* 2:50-58 (Jan) 1946.
85 Cummings, Roland: Obesity and its treatment. *California & West. Med.* 29:41-42 (July) 1928.
86. Currier, F P., and Davis, D B : Progressive lipodystrophy appearing at menopause. *Am. J. M. Sc.* 179:750-758 (June) 1930.
87 Cushing, Harvey: *The pituitary body and its disorders.* Philadelphia, J. B. Lippincott Company, 1912, 341 pp.
88. Cutting, W. C.: The treatment of obesity. *J. Clin. Endocrinol* 3:85-88 (Feb) 1943.
89. Cutting, W. C.: The coexistence of obesity and narcolepsy, a consideration of the etiology of obesity. *Stanford M. Bull.* 2:172-175 (Nov.) 1944.
90. Danforth, C H : Hereditary adiposity in mice *J. Hered.* 18 153-162 (Apr.) 1927.
91 Danowski, T. S., and Winkler, A. W.: Obesity as a clinical problem *Am. J. M. Sc.* 208·622-630 (Nov.) 1944.
92. Davenport, C. B.: *Body-build and its inheritance.* Washington, D C., Carnegie Institution of Washington, 1923, 176 pp
93. Davidoff, Eugene: A comparison of the stimulating effect of amphetamine, dextroamphetamine and dextro-N-methyl amphetamine (dextro-desoxyephedrine). *M. Rec.* 156. 422-424 (July) 1943.
94 Davidoff, L M.· Endocrinologic aspects of tumors of pineal gland *Surgery.* 16·306-314 (Aug) 1944.
95. Davis, Clara M : Results of the self-selection of diets by young children *Canad M A.J.* 41:257-261 (Sept) 1939.
96. Davis, Loyal, and Martin, John: Results of experimental removal of pineal gland in young mammals. *Arch Neurol. & Psychiat.* 43:23-45 (Jan.) 1940.
97 Dercum, F. X.: Three cases of a hitherto unclassified affec-

tion resembling in its grosser aspects obesity, but associated with special nervous symptoms — adiposis dolorosa *Am J. M. Sc.* 104:521-535 (Nov.) 1892.

98 Dercum, F X, and McCarthy, D. J Autopsy in a case of adiposis dolorosa *Am. J. M Sc.* 124·994-1006 (Dec) 1902

99 Dey, F L. Evidence of hypothalamic control of hypophyseal gonadotropic functions in female guinea pig *Endocrinology.* 33.75-82 (Aug) 1943

100. Dickerson, G E, and Gowen, J W Food utilization in genetic obesity of mice *Genetics* 31 214-215 (Mar) 1946

101 Dickerson, Virginia C, Tepperman, Jay, and Long, C N H The rôle of the liver in the synthesis of fatty acids from carbohydrate *Yale J Biol & Med* 15 875-892 (July) 1943.

102. Douthwaite, A H.: The treatment of obesity *Brit M J* 2·344-346 (Aug 15) 1936

103 Drury, D. R: The rôle of insulin in carbohydrate metabolism *Am J. Physiol* 131 536-543 (Dec) 1940

104 Dublin, L I· The influence of weight on certain causes of death *Human Biol.* 2·159-184 (May) 1930

105 Dublin, L I, and Marks, H H· *Mortality of women according to build—experience on substandard issues* New York City, Press of Recording and Statistical Corporation, 1939, 22 pp

106 Dublin, L I, Fisk, E L, and Kopf, E W· Physical defects as revealed by periodic health examinations *Am J M Sc* 170·576-594 (Oct) 1925

107. DuBois, E F. *Basal metabolism in health and disease Ed 2,* Philadelphia, Lea & Febiger, 1927, p 235

108 DuBois, E F *Basal metabolism in health and disease Ed 3,* Philadelphia, Lea & Febiger, 1936, 494 pp

109. DuBois, E F, Spencer, H J, McClellan, W S, and Falk, E The specific dynamic action of protein in the obese *J Clin. Investigation* 7 499 (May 6) 1929

110 Duncan, G G.· *Diseases of metabolism.* Philadelphia, W. B Saunders Company, 1942, p 500

111. Dunlop, D. M, and Lyon, R. M M. A study of 523 ca obesity *Edinburgh M. J* 38 561-577 (Oct) 1931.

112. Dunlop, G R.: Saphenous (ligation) resection in *Ann. Surg* 118:1024-1031 (Dec) 1943

113. Dunlop, H. A.: Body weight in health and disease *Post-Grad. M. J.* 14:176-183 (June) 1938.

114. Eaves, Elizabeth C, and Croll, Margaret M: The pituitary and hypothalamic region in chronic epidemic encephalitis *Brain* 53 56-75 (Apr) 1930.

115. Editorial: A study of impairments found among 10,000 unselected examinees. Article II: Weight. *Proc. Life Ext. Exam.* 1:89-93 (July-Aug) 1939.

116 Editorial What are the practical limits of weight reduction? *Proc. Life Ext. Exam.* 3:99-110 (Sept.-Oct) 1941.

117. Editorial: Primitive fat organs *J.A M.A.* 133:1283 (Apr 26) 1947.

118. Eidelsberg, Joseph: Obesity; procedure, classification, treatment, and results, in 151 cases studied during the past six years, with special reference to an endocrinopathic origin *Ann. Int Med.* 3:604-607 (Dec.) 1929.

119. Emerson, G. A: Amphetamine for obesity. *J.A M.A.* 122:268 (May 22) 1943.

120 Emerson, G A.: Relative effects of *d*- and *l*-amphetamine on metabolic rate in man. *Federation Proc.* 3:71 (Mar.) 1944.

121. Engelbach, William: *Endocrine medicine* Springfield, Illinois, Charles C Thomas, 1932, vol 3, 862 pp

122 Epstein, A A: Clinical and biologic considerations of obesity and certain allied conditions. *Bull. New York Acad. Med.* 10:389-414 (July) 1934.

123. Ersner, J S: The treatment of obesity due to dietary indiscretion (overeating) with benzedrine sulfate *Endocrinology* 27 776-780 (Nov.) 1940

124 Evans, F A.: Treatment of obesity with low calory diets. report of 121 additional cases. *Internat. Clin.* 3:19-23 (Sept) 1938

125 Evans, F A: Obesity. In Duncan, G. G.: *Diseases of metabolism.* Philadelphia, W. B Saunders Company, 1942, pp. 513-591.

126 Evans, F A, and Strang, J. M.: A departure from the usual methods in treating obesity. *Am. J. M Sc.* 177:339-348 (Mar.) 1929.

127. Evans, F. A, and Strang, J. M: The treatment of obesity with low caloric diets. *J.A.M A.* 97:1063-1068 (Oct. 10) 1931

128. Farquharson, R. F., and Squires, A. H: Inhibition of the

secretion of the thyroid gland by continued ingestion of thyroid substance. *Tr. A. Am. Physicians.* 56 87-97, 1941

129 Faust, R. A: Complications of obesity *New Orleans M & S. J.* 98 502-507 (May) 1946.

130 Feinblatt, H. M: Report of clinical and toxicity investigations with thyrobrom for weight reduction *M Rec* 158 420-422 (July) 1945

131 Fellows, H H. Studies of relatively normal obese individuals during and after dietary restrictions *Am J M Sc* 181 301-312 (Mar.) 1931

132 Fetter, Ferdinand, Durkin, J K., and Duncan, G G. Dietary versus insulin treatment of the obese diabetic patient *Am. J M Sc.* 195 781-787 (June) 1938

133. Fleming, R G, and Snell, A M · Portal cirrhosis with ascites: an analysis of 200 cases with special reference to prognosis and treatment. *Am J Digest Dis.* 9.115-120 (Apr) 1942.

134 Folin, Otto, and Denis, W: On starvation and obesity, with special reference to acidosis. *J. Biol Chem* 21 183-192, 1915.

135. Frazier, C. H: Pituitary cachexia *Arch Neurol & Psychiat* 21:1-18 (Jan) 1929

136 Frazier, C H · Tumor involving the frontal lobe alone, a symptomatic survey of one hundred and five verified cases *Arch. Neurol. & Psychiat* 35 525-571 (Mar) 1936

137. Freed, S C: Psychic factors in the development and treatment of obesity *J.A.M A* 133 369-373 (Feb 8) 1947

138. Freyberg, R. H · A study of the value of insulin in undernutrition *Am. J M Sc* 190.28-42 (July) 1935

139. Freyberg, R. H, and Newburgh, L H The obesity and energy exchange in a verified case of pituitary basophilism *Arch. Int. Med.* 58 229-234 (Aug) 1936.

140 Gamble, J L *Chemical anatomy, physiology and pathology of extracellular fluid; a lecture syllabus.* Cambridge, Massachusetts, Department of Pediatrics, The Harvard Medical School, 1942, 120 pp

141. Gardiner-Hill, H., Jones, I., and Smith, J F Pituitary obesity in adolescence. *Quart. J Med.* 18 309-326, 1925

142. Gericke, O. L.: Suicide by ingestion of amphetamine sulfate *J A M A* 128 1098-1099 (Aug 11) 1945.

143 Gibbons, Rebekah: On the specific dynamic action of proteins

in thin and fat individuals (dogs). *Am. J. Physiol.* 70: 26-28 (Sept.) 1924.

144. Gildea, E. F., and Man, Evelyn B.: Hypothalamus and fat metabolism. In *Association for Research in Nervous and Mental Diseases*: The hypothalamus and central levels of autonomic function. Baltimore, The Williams & Wilkins Company, 1940, vol. 20, pp. 501-524.

145. Gill, Dorothy J.: The role of personality and environmental factors in obesity. *J. Am. Dietet. A.* 22:398-400 (May) 1946

146 Godlowski, Zbigniew: Carbohydrate metabolism in obesity *Edinburgh M. J* 53:574-582 (Oct.) 1946.

147 Goldzieher, J. W.: Pituitary lesions accompanying obesity. *Arch. Path.* 41.203-212 (Feb) 1946.

148. Goldzieher, M A.: *The endocrine glands.* New York, D. Appleton-Century Company, 1939, 916 pp

149 Goldzieher, M. A.: Endocrine aspects of obesity. *Am. J. Digest. Dis.* 13:40-54 (Feb) 1946.

150 Gordon, Burgess and von Stanley, E.: The use of dextrose in the treatment of obesity. With special reference to the reduction of the body weight without markedly lowering the daily caloric intake. *Am. J. M. Sc.* 175:37-43 (Jan) 1928

151 Gordon, M B.: Endocrine obesity in children: clinical and laboratory studies and results of treatment. *J. Pediat.* 10. 204-220 (Feb.) 1937.

152 Grafe, Erich: *Metabolic diseases and their treatment.* Philadelphia, Lea & Febiger, 1933, 551 pp.

153 Grafe, E., and Graham, D.: Über die Anpassungsfähigkeit des tierischen organismus an überreichliche Nahrungszufuhr (nach Versuchen am Hunde). *Ztschr. f. physiol. Chem.* 73:1-67, 1911.

154. Gray, Horace: Obesity in the adolescent cured without injections. *J.A.M.A.* 110:1430-1433 (Apr. 30) 1938.

155 Gray, Horace, and Kallenbach, Dorothy E. Obesity treatment: results on 212 outpatients. *J. Am. Dietet. A.* 15: 239-245 (Apr) 1939.

156 Greene, J. A. Clinical study of the etiology of obesity. *Ann. Int. Med* 12:1797-1803 (May) 1939.

157. Greene, J A.: The effect of belladonna on the appetite of patients with obesity and with other diseases. *J. Lab. & Clin. Med.* 26.477-478 (Dec.) 1940.

158 Greene, Raymond: Adiposity. *Post-Grad. M. J* 22 169-181 (June) 1946

159 Greenhill, J. P.: *Office gynecology, Ed 3,* Chicago, Year Book Publishers, 1940, 424 pp.

160. Grimm, E G · Obesity and endocrine glands. *Mississippi Valley M. J.* 65:130-132 (Oct.) 1943.

161. Grollman, Arthur, and Rousseau, J P. Metabolic craniopathy; a clinical and roentgenologic study of so-called hyperostosis frontalis interna *J.A M A.* 126 213-217 (Sept. 23) 1944.

162 Grossman, M I, Cummins, G M., and Ivy, A. C.· The effect of insulin on food intake after vagotomy and sympathectomy. *Am J Physiol.* 149.100-102 (Apr) 1947.

163. Gulick, Addison: A study of weight regulation in the adult human body during over-nutrition *Am. J Physiol* 60 371-395 (Apr) 1922

164 Gurney, Ramsdell. The hereditary factor in obesity *Arch. Int. Med.* 57.557-561 (Mar) 1936.

165. Hagedorn, H. C, Holten, C., and Johansen, A H The pathology of metabolism in obesity *Arch Int Med* 40 30-37 (July) 1927

166 Handelsman, M B : Factors influencing the return of tolerance for glucose in middle-aged obese diabetics *Am J M Sc.* 208·15-24 (July) 1944

167. Handelsman, M B, and Gordon, M B The calorigenic action of thyroid substance in obese patients *J Clin Endocrinol.* 1·612-619 (July) 1941

168 Harris, S C., and Ivy, A. C The influence of extrinsic gastro-intestinal innervation on dexedrine induced anorexia *Federation Proc.* 5:42 (Feb) 1946.

169. Harris, S C, Ivy, A. C., and Searle, Laureen M The mechanism of amphetamine-induced loss of weight, a consideration of the theory of hunger and appetite. *J.A M A* 134 1468-1475 (Aug 23) 1947

170. Hawirko, Leonora, and Sprague, P H Treatment of obesity by appetite-depressing drugs *Canad M A J* 54 26-29 (Jan) 1946.

171. Heinbecker, Peter, White, H. L, and Rolf, Doris· Experimental obesity in the dog *Am J Physiol.* 141.549-565 (Feb 4) 1944.

172. Herrick, W. W.: Hypertension and hyperglycemia *J.A M A.* 81·1942-1944 (Dec. 8) 1923

173. Hess, J H., and Kunstadter, R. H.: Diagnosis and treatment of obesity in children. *M. Clin. North America* 22: 161-180 (Jan.) 1938.
174. Hetenyi, G.: Untersuchungen über die Entstehung der Fettsucht. *Deutsches Arch. f. klin. Med.* 179:134-141, 1936.
175. Hetherington, A. W.: The production of hypothalamic obesity in rats already displaying chronic hypopituitarism. *Am. J Physiol.* 140:89-92 (Oct.) 1943.
176. Hetherington, A. W., and Ranson, S W.: Hypothalamic lesions and adiposity in the rat. *Anat Rec.* 78:149-172 (Oct) 1940.
177. Hetherington, A. W., and Ranson, S W.: Effect of early hypophysectomy on hypothalamic obesity. *Endocrinology.* 31:30-34 (July) 1942.
178. Hill, Joel: Infant feeding and personality disorders; a study of early feeding in its relation to emotional and digestive disorders *Psychiatric Quart.* 11:356-382 (July) 1937.
179. Hirsh, L S: Controlling appetite in obesity *J. Med.* 20:84-85 (Apr) 1939.
180. Hochman, Samuel: Mental and psychological factors in obesity *M. Rec.* 148:108-111 (Aug 3) 1938.
181. Hoff, H. E: Physiology *New England J. Med.* 235:826-830 (Dec 5) 1946.
182. Hoffman, Jacob: *Female endocrinology including sections on the male.* Philadelphia, W. B. Saunders Company, 1944, 788 pp.
183. Hollander, Franklin: The insulin test for the presence of intact nerve fibers after vagal operations for peptic ulcer. *Gastroenterology.* 7:607-614 (Dec.) 1946
184. Hutchinson, Robert, and Gardiner-Hill, H.: Body weight in relation to disease. *Tr. M. Soc. London.* 33:112-123 (Feb 11) 1935.
185. Ingle, D. J.: Relationship of the adrenal cortex to the metabolism of fat. *J. Clin. Endocrinol.* 3:603-612 (Nov) 1943.
186. Ishmael, W. K.: The familial aspects of gout, diabetes mellitus and obesity *J. Oklahoma M. A.* 38:415-418 (Oct.) 1945.
187. Ivy, A C, and Goetzl, F. R.: d-Desoxyephedrine, a review. *War. Med.* 3:60-77 (Jan) 1943.
188 Jarlov, Ejnar. Clinical types of abnormal obesity. *Acta med. Scandinav.* (suppl.) 42:1-70, 1932.

189 Jaso, E, and Curbelo, A. A: Contribution to knowledge of Laurence-Moon-Biedl syndrome, three cases of monstrous infantile obesity *Am J. Dis. Child.* 70 9-18 (July) 1945

190 Jenkins, R L, and Poncher, H G. Pathogenesis of the Laurence-Biedl syndrome *Am J. Dis Child.* 50 178-186 (July) 1935

191. Johnson, W M: Different weight responses to the same provocation *J A M A.* 133:1238 (Apr 19) 1947.

192 Johnston, J. A, and Maroney, J W.. Relationship of basal metabolism to dietary intake *Am J Dis. Child* 51 1039-1051 (May) 1936

193 Johnston, Margaret W., and Newburgh, L. H · The determination of the total heat eliminated by the human being *J Clin Investigation* 8 147-160 (Feb) 1930

194 Jones, H M · Basal metabolic rate in simple and pathologic obesity *J Lab. & Clin Med* 11 959-967 (July) 1926

195 Jones, L J, and Boines, G J: Rehabilitation in the obese by lipectomy *Delaware State M J* 18 161-162 (July) 1946

196 Joslin, E P, Dublin, L I., and Marks, H H Studies in diabetes mellitus. III Interpretation of the variations in diabetes incidence. *Am. J M Sc* 189 163-192 (Feb) 1935

197 Kain, Ida J. Safe and sane reducing diets *J Am. Dietet A* 17.671-674 (Aug-Sept) 1941

198 Kalb, S W. Amphetamine (benzedrine) sulphate and thyroid extract in the treatment of obesity observations on 500 cases *J. M Soc New Jersey* 39.74-75 (Feb) 1942

199 Kalb, S W: Effects of various thyroid substances in patients with obesity *J. Clin Endocrinol* 3 7-11 (Jan) 1943

200 Kalb, S W.: The fallacy of massage in the treatment of obesity *J M. Soc. New Jersey* 41 406-407 (Nov) 1944

201 Keeton, R. W, and Dickson, Dorothy· Excretion of nitrogen by obese patients on diets low in calories, containing varying amounts of protein *Arch. Int. Med.* 51 890-902 (June) 1933.

202. Keller, A D, and Noble, William: Adiposity with normal sex function following extirpation of the posterior lobe of the hypophysis in the dog *Am. J. Physiol* 113 79-80 (Sept) 1935

203 Keller, A D, and Noble, W.: Further observations on enhanced appetite with resultant adiposity following removal

of the posterior lobe of the hypophysis. *Am. J. Physi* 116:90-91 (June) 1936.

204 Keller, A D., Noble, William and Hamilton, J. W., Jı Effects of anatomical separation of the hypophysis fro the hypothalamus in the dog. *Am. J. Physiol.* 117.46 473 (Nov) 1936.

205. Kelley, W H · Portal cirrhosis in the obese. *South. M.* 39:978-981 (Dec.) 1946.

206. Kemper, C F.: Obesity — its significance and treatmen *Rocky Mountain M. J.* 37:835-840 (Nov.) 1940.

207. Kennard, Margaret A., Spencer, S. [illegible] and Fountain, G. Jr. [illegible]

208 Kern, Maximilian: Further studies in the problems of obesity *Arch Phys Therapy.* 11·418-426 (Aug.) 1930.

209. Kerr, W. J., and Lagen, J. B.: The postural syndrome related to obesity leading to postural emphysema and cardiorespiratory failure *Ann Int. Med.* 10 569-595 (Nov.) 1936

210. Keys, Ancel· *Personal communication to the authors.*

211. Kisch, Franz: Über die Ebsucht Schweradipöser. *Ztschr. f. klin Med* 132 504-513 (Apr.) 1937.

212 Knies, P T, and Le Fever, H. E.: Metabolic craniopathy: hyperostosis frontalis interna *Ann Int Med* 14:1858-1892 (Apr.) 1941.

213. Krantz, C. I, and Means, J. H.: The effect of epinephrin on the partition of food stuffs in obese and normal individuals *J. Clin. Investigation.* 4·225-233 (June) 1927.

214. Kraus, J E · Hyperplastic disease of the adenohypophysis *J. Clin. Endocrinol* 5.42-51 (Jan) 1945.

215. Kraus, J. E : Morphologic aspects and genesis of disorders of adenohypophysis *Arch. Path.* 40:191-207 (Sept) 1945

216. Krause, A K.. Factors in the pathogenesis of tuberculosis; with a preliminary discussion of activity. *Am. Rev. Tuberc.* 18 208-248 (Aug) 1928

217. Kunstadter, R. H.: Experience with benzedrine sulfate in the management of obesity in children. *J. Pediat.* 17:490-501 (Oct) 1940.

218. Kunstadter, R. H., and Necheles, H : Studies on the effect and mechanism of amphetamine sulfate on weight reduction *Am J. M. Sc.* 205.820-825 (June) 1943.

219 Lagen, J. B., Soley, M. H., and Leake, T B.: Effect of benze-

drine sulfate on basal metabolic rate *Proc Soc. Exper. Biol. & Med.* 35 276-278 (Nov) 1936

220 Langeron, L, Paget, M, and Ledieu, J. Sur l'action des extraits thyroïdien et hypophysaire sur la composition du sang et sur la diurése Action conjuguée de l'extrait thyroïdien et de la théobromine *Bull Acad de méd, Paris* 109 843-846 (Apr) 1933

221 Lauter, S Zur Genese der Fettsucht *Deutsches Arch f klin Med* 150 315-365 (Mar) 1926

222. Lauter, S, and Terhedebrugge, A. Über Fettansatz und Fett verteilung bei Fettsuchtigen *Deutsches Arch. f. klin Med* 183.91-108 (Oct 14) 1938

223 Lawrence, H E Obesity, mental retardation, polydactyly, retinal pigmentation and hypogenitalism (Laurence-Moon-Biedl syndrome); case report *Bull New England M Center* 6 285-290 (Dec) 1944

224 Lawrence, R D Lipodystrophy and hepatomegaly with diabetes lipaemia, and other metabolic disturbances, a case throwing new light on the action of insulin *Lancet* 1 724-731, 773-775 (May 25) 1946

25 Leech, P N, Council on Pharmacy and Chemistry, reports of the council Dinitrophenol not acceptable for N N R *J A M A* 105 31-33 (July 6) 1935

226 Lesses, M F, and Myerson, Abraham Human autonomic pharmacology XVI Benzedrine sulfate as an aid in the treatment of obesity *New England J Med* 218 119 121 (Jan 20) 1938

227. Levy, R L, White, P D, Stroud, W D, and Hillman, C C Overweight, its prognostic significance in relation to hypertension and cardio-vascular-renal diseases *J A M A* 131 951-953 (July 20) 1946

228 Ley, H A The effect of change in weight on blood pressures as shown in a study of 3,516 examinees *Proc Life Ext. Exam.* 1 33-36 (Mar-Apr) 1939

29 Lichtwitz, L Über die Beziehungen der Fettsuch zu Psyche und Nervensystem *Klin Wchnschr* 2 1255-1257 (July) 1923

0 Lightwood, Reginald Tumour of the suprarenal cortex in an infant of 18 weeks *Arch. Dis Childhood.* 7 35-42, 1932

Long, C N H, Katzin, B, and Fry, Edith G: The adrenal cortex and carbohydrate metabolism *Endocrinology* 26 309-344 (Feb) 1940

232. Lusk, Graham: The physiological effect of undernutrition. *Physiol Rev.* 1:523-552 (Oct.) 1921.

233. Lyon, D. M.: Diet in health and disease; diet in endocrine disorders and obesity. *Practitioner.* 140,68-76 (Jan) 1938.

234 Lyon, D M., and Dunlop, D. M · The treatment of obesity; a comparison of the effects of diet and of thyroid extract. *Quart. J. Med.* 1:331-352 (Apr.) 1932.

235. Lyon, D M, Dunlop, D. M., and Stewart, C P.: Respiratory quotient in obese subjects *Biochem. J.* 26:1107-1117 (Apr. 2) 1932.

236. Lyon, I. P.: Adiposis and lipomatosis. *Arch. Int. Med* 6: 29-120 (Aug.) 1910.

237 McCann, W S.: The dietary requirements in pulmonary tuberculosis *Am. Rev. Tuberc.* 5:870-875 (Jan.) 1922

238 McClugage, H. B., Booth, George, and Evans, F. A.: Creatinin excretion in abnormal states of nutrition. *Am J. M Sc* 181 349-355 (Mar.) 1931.

239 McCord, C P The pineal gland; the influence of the pineal gland upon growth and differentiation with particular reference to its influence upon prenatal development. *Surg., Gynec & Obst.* 25.250-260 (Sept.) 1917.

240 McCullagh, E P.: Management of obesity. *Ohio State M. J.* 34.1131-1135 (Oct.) 1938.

241. McCune, D. J, and Bruch, Hilde: Basal metabolism of children. critical interpretation based on observations in obese subjects *Am J. Dis. Child.* 72·457-459 (Oct.) 1946

242. MacKay, E M, and Barnes, R. H: Influence of adrenalectomy on the ketosis of fasting and on the action of the anterior pituitary ketogenic principle. *Am. J. Physiol.* 118: 184-189 (Jan) 1937.

243 MacKay, E M., and Sherrill, J W.: A comparison of the ketosis developed during fasting by obese patients and normal subjects. *Endocrinology.* 21.677-680 (Sept.) 1937.

244 MacKay, E. M., and Sherrill, J W.: Influence of thyroidectomy on fat deposition in the rat. *Endocrinology.* 28:518 (Mar) 1941

245. MacKay, E. M., Callaway, J. W., and Barnes, R. H.: Hyperalimentation in normal animals produced by protamine insulin. *J. Nutrition.* 20.59-66 (July) 1940.

246 Maclagen, N F. · The rôle of appetite in the control of body weight. *J. Physiol.* 90·385-391 (Sept 17) 1937

247. Marañon, G, and Soler, J. B · Progressive lipodystrophy and hyperthyroidism *Endocrinology.* 10 1-16 (Jan -Feb) 1926.

248 Marks, T M, Thomas, J M, and Warkany, J Adreno-cortical obesity in children *Am J. Dis Child* 60 923-942 (Oct) 1940

249. Matlow, A. A., and Callaway, J W · The use of protamine zinc insulin in undernutrition Quoted by MacKay, E M, Callaway, J W, and Barnes, R H.[88]

250 Marmor, Judah, and Lambert, R K Laurence-Moon-Biedl syndrome, its relation to the general problem of retinitis pigmentosa *Arch. Int. Med* 61 523-536 (Apr) 1938

251. Mason, E C, and Hellbaum, A A Acid-base water balance *Ann. Int. Med* 11 2206-2213 (June) 1938

252. Mason, E H The treatment of obesity *Canad M A J* 14 1052-1056 (Nov) 1924

253. Mason, E H Abnormal specific dynamic action of protein, glucose, and fat associated with undernutrition *J Clin Investigation.* 4 353-384 (Apr 18) 1927

254 Master, A. M, and Oppenheimer, E T · A study of obesity, circulatory, roentgen-ray and electrocardiographic investigations *J A M A* 92·1652-1656 (May 18) 1929

255. Master, A M, Jaffe, H L, and Dack, S. A study of 150 cases of coronary thrombosis treated with low calorie diets *Am Heart J.* 10 1102 (Dec) 1935.

256 Master, A M, Jaffe, H L, and Dack, S Undernutrition in the treatment of coronary artery disease (particularly thrombosis). Effect on the basal metabolism and circulation *J. Clin Investigation.* 15.353-367 (July) 1936

257 Master, A M, Stricker, Jenny, Grishman, Arthur, and Dack, Simon · Effect of undernutrition on cardiac output and cardiac work in overweight subjects *Arch. Int. Med* 69 1010-1018 (June) 1942

258 Matthews, H B, and Der Brucke, M G "Normal expectancy" in the extremely obese pregnant woman *J. A M. A.* 110 554-558 (Feb 19) 1938

259. Means, J H. Studies of the basal metabolism in obesity and pituitary disease *J M Res.* 32 121-158 (Mar.) 1915

260 Means, J H · The basal metabolism in obesity. *Arch. Int Med* 17 704-710 (May) 1916.

261. Means, J H: Therapeutics of the thyroid *J.A.M.A.* 105: 24-28 (July 6) 1935.
262. Metropolitan Life Insurance Company: Girth and death. *Metropolitan Life Insurance Stat. Bull.* 18:2-5 (May) 1937.
263 Metropolitan Life Insurance Company: Ideal weights for women *Metropolitan Life Insurance Stat. Bull.* 23 6-8 (Oct.) 1942
264 Metropolitan Life Insurance Company. Ideal weights for men *Metropolitan Life Insurance Stat. Bull.* 24:6-8 (June) 1943.
265 Metropolitan Life Insurance Company *Overweight and underweight.* New York, 32 pp.
266 Mirski, A · Metabolism of adipose tissue *in vitro. Biochem J* 36·232-241 (Jan. 26) 1942.
267 Mittelmann, Bela: Juvenile adiposogenital dystrophy Neurologic and psychopathologic aspects Results of organotherapy and psychotherapy. *Endocrinology.* 23·637-655 (Nov) 1938
268. Moller, Eggert: Results of exclusively dietary treatment in 46 cases of obesity. *Acta med. Scandinav* 74:341-352, 1931
269 Moore, M. T.: Morgagni-Stewart-Morel syndrome, report of case with pneumoencephalographic findings *Arch. Int. Med.* 73·7-12 (Jan.) 1944
270 Moore, Sherwood: Metabolic craniopathy. *Am. J. Roentgenol* 35·30-39 (Jan) 1936.
271. Moore, Sherwood: Calvarial hyperostosis and the accompanying symptom complex *Arch. Neurol. & Psychiat.* 35:975-981 (May) 1936
272. Morgulis, Sergius: *Fasting and undernutrition; a biological and sociological study of inanition.* New York, E P. Dutton & Company, 1923, 407 pp.
273. Mortimer, H. Influence of anterior pituitary on cranial form and structure and significance of cranial dysplasia in clinical diagnosis. *Proc. A. Research Nerv. & Ment Dis.* 17: 222-238, 1938
274 Moschcowitz, Eli. Essays on the biology of disease. obesity. *J. Mt. Sinai Hosp* 11:357-367 (Mar-Apr) 1945.
275. Mulier, Hannah, and Topper, Anne: Treatment of obesity in a group of children *Am. J. Dis. Child.* 47·25-33 (Jan.) 1934.
276 Musser, J H, and Wright, D. O.: Hypertension, obesity and

hyperglycemia. *J A M A.* [illegible]

277. Myerson, Abraham Neuroses [illegible] lationship of symptom gro[illegible] 301 (Sept) 1936

278 Myerson, Abraham, Loman, J[illegible] Physiologic effects of benz[illegible] other drugs affecting the [illegible] *J M Sc* 192 560-574 (Oc) [illegible]

279 Nahum, L H, and Himwich, H [illegible] I A method for increasing [illegible] *J M Sc* 183 608 613 (Ma[illegible]) [illegible]

280. National Research Council Boa[illegible] *Recommended dietary allowa*[illegible] Series 122, August, 1945.

281 Neuenschwander-Lemmer, Nelly: [illegible] bei fettsuchtigen und normalen [illegible] *exper Med* 99 394-398 (July [illegible]

282 Newburgh, L H The cause of [illegible] 1661 (Dec 5) 1931

283 Newburgh, L H Control of hy[illegible] betics" by weight reduction *Ann* [illegible] (Dec) 1942

284 Newburgh, L H Obesity *Arch.* [illegible] (Dec) 1942

285 Newburgh, L H Obesity *J* [illegible] *Rev* 24 18-31 (Jan) 1944.

286 Newburgh, L H, and Conn, J W [illegible] hyperglycemia in obese middle [illegible] 112 7-10 (Jan 7) 1939

87 Newburgh, L H, and Johnston, M[illegible] obesity — a misconception. *Ann.* [illegible] (Feb) 1930.

288 Newburgh, L H, and Johnston, M[illegible] of obesity *J Clin Investigation* [illegible]

289 Newburgh, L H, and Johnston, M[illegible] *M Clin North America* 27.227 [illegible]) 193[illegible]

290 Newburgh, L H, Johnston, Marga[illegible] J D *Some fundamental principle*[illegible] Ann Arbor, Edwards Brothers, Inc, [illegible]

291 Nicholson, W M Emotional facto[illegible] *Sc* 211 443-447 (Apr) 1946. [illegible]

292 Norman, Jacob, and Shea, J T [illegible] *Am. J.* [illegible]

plication of addiction to amphetamine sulfate; report of a case. *New England J. Med.* 233:270-271 (Aug 30) 1945.
293. Novelli, A M, and Tainter, M. L.: The stimulant power of secondary and tertiary phenyl-isopropyl-amines *J. Pharmacol. & Exper. Therap.* 77:324-331 (Apr.) 1943.
294. Odell, L. D, and Mengert, W. F.: Overweight, obstetric patient *J.A.M A.* 128.87-90 (May 12) 1945.
295 Ogilvie, R. F: Sugar tolerance in obese subjects· a review of sixty-five cases *Quart. J. Med.* 4:345-358 (Oct) 1935
296 Ornsteen, A M: A contribution to the pathogenesis and heredity of the Laurence-Biedl syndrome (dystrophia adiposogenitalis, retinitis pigmentosa, mental deficiency and polydactylism); report of three cases in one family. *Am. J. M. Sc.* 183:256-268 (Feb.) 1932.
297. Parmelee, A. H.. Lipodystrophy; a report of six cases in children *J.A.M.A.* 98:548-552 (Feb 13) 1932.
298 Pelner, Louis The management of obesity. *New York State J Med.* 44:2596-2598 (Dec. 1) 1944
299 Pelner, Louis· The treatment of obesity by appetite control: the use of autonomic substances and their synergists *Ann Int. Med.* 22:201-212 (Feb) 1945.
300 Pelner, Louis: *The management of obesity.* New York, Personal Diet Service, 1946, 142 pp
301 Peters, J. P, and Van Slyke, D. D· *Quantitative clinical chemistry interpretations. Ed. 2,* Baltimore, The Williams & Wilkins Company, 1946, vol. 1, 1041 pp.
302 Plummer, W A· Body weight in spontaneous myxedema *Tr. Am. A Study Goiter,* pp. 88-98, 1940
303 Potter, V. R. The rôle of nutrition in cancer prevention *Science.* 101.105-109 (Feb. 2) 1945.
304. Preble, W E: Obesity: observations on one thousand cases *Boston M & S. J.* 188:617-621 (Apr. 26) 1923.
305 Prinzmetal, M, and Alles, G A: The central nervous system stimulant effects of dextro-amphetamine sulfate. *Am. J. M. Sc* 200.665-673 (Nov) 1940.
306 Prodger, S H, and Dennig, H.· A study of the circulation in obesity. *J Clin. Investigation.* 11·789-806 (July) 1932
307. Raab, W· Klinische und röntgenologische Beiträge zur hypophysären und zerebralen Fettsucht und Genitalatrophie *Wien. Arch. f inn. Med* 7·443, 1924
308. Raab, W: Das Hypophysen-zwischenhirnsystem und seine

pituitary gland Baltimore, Williams & Wilkins Company, *1938*, vol *17*, pp *69-117*

338 Sevringhaus, E L Diagnostic and therapeutic problems of obesity *J Michigan M Soc* 42 530-536 (July) 1943

339 Sevringhaus, E. L: *Endocrine therapy in general practice Ed 5* Chicago, The Year Book Publishers, Inc, 1945, 253 pp

340. Seward, B P A clinical study of the mild grades of hypothyroidism *Ann Int. Med* 9 178-188 (Aug) 1935

341. Sheehan, H L Simmonds' disease due to post-partum necrosis of the anterior pituitary *Quart J Med n s* 8 277-309 (Oct) 1939

342 Shepardson, H C . Insulin fattening in ambulatory patient *California & West Med* 40 14-18 (Jan) 1934

343 Short, J J Increasing weight with insulin, preliminary report *J Lab & Clin Med* 14 330-335 (Jan) 1929

344 Short, J J Extreme obesity followed by therapeutic reduction of two hundred and thirty-nine pounds *J A M A* 111·2196-2197 *(Dec 10) 1938*

345 Short, J J Increase of electrocardiographic changes with obesity *Proc Life Ext Exam* 1 82-85 (July-Aug) *1939*

346 Short, J J · The effect of increasing age on the blood pressures of 9,926 individuals according to sex and weight groups *Proc Life Ext Exam.* 2 35-40 (Mar -Apr) 1940

347 Short, J J Obesity In Bridges, M A · *Dietetics for the clinician Ed 4*, Philadelphia, Lea & Febiger, 1941, p 463

348 Short, J J, *and Currence, J DeP . An attempt to mobilize* lipoids from storage depots by deep massage and increased tissue temperatures *J Lab & Clin Med* 24 395-397 (Jan) 1939

349 Short, J J, and Johnson, H J · The increased metabolism of obesity, use and abuse of metabolic stimulants *J A. M A* 106·1776-1779 (May 23) 1936.

350 Short, J J, and Johnson, H. J The effect of overweight on vital capacity. *Proc Life Ext Exam.* 1 36-41 (Mar -Apr) 1939

351. Short, J J, and Johnson, H J [illegible] aluation of the influence of overweight on blood [illegible] f healthy men; a study of 3516 individuals [illegible] health examinations [illegible] *Sc. 198* [illegible] Aug) 1939

352 Shorvon, [illegible] te by [illegible]

324. Rosenthal, Gerhard, and Solomon, H A.: Benzedrine sulfate in obesity. *Endocrinology.* 26 807-812 (May) 1940.

325. Ross, T A · *The common neuroses; their treatment by psychotherapy;* an introduction to psychological treatment for students and practitioners. Baltimore, William Wood & Company, 1937, 236 pp

326 Rowntree, L G, and Brunsting, L. A.: Water or fat? Water retention in so-called endocrine obesity *Endocrinology,* 17.377-382 (July-Aug.) 1933.

327 Russell, W O, and Sachs, Ernest: Pinealoma, a clinicopathologic study of seven cases with a review of the literature. *Arch. Path.* 35:869-888 (June) 1943.

328. Rynearson, E. H : The problem of obesity *Proc. Inst. Med. Chicago.* 15·35-37 (Jan 15) 1944.

329 Rynearson, E H, and Hildebrand, Alice G : Metabolism and diabetes; review of certain recent contributions. *Arch. Int Med* 68 134-175 (July) 1941.

330 Rynearson, E H, and Sprague, Anne W.: Obesity. *California & West. Med.* 53·158-162 (Oct) 1940.

331 Rytand, D A · Hereditary obesity of yellow mice, a method for the study of obesity *Proc. Soc. Exper. Biol. & Med* 54 340-341 (Dec) 1943

331a Schneeberg, N G, Woolhandler, George, and Levine, Rachmiel. The clinical significance of hyperostosis frontalis interna. *J Clin Endocrinol.* 7·624-635 (Sept) 1947.

332 Schoenheimer, Rudolph: The investigation of intermediary metabolism with the aid of heavy hydrogen. *Harvey Lect.* 32:122-144, 1936-1937.

333. Schopbach, R R, and Matthews, R. A : Psychologic factors in the problem of obesity. *Arch. Neurol. & Psychiat.* 54·157-158 (Aug) 1945.

334. Schultz, F W : What to do about the fat child at puberty *J. Pediat.* 19.376-381 (Sept.) 1941.

335 Schulte, J W. Reif, E C., Bacher, J. A, Jr, Lawrence, W S, and Tainter, M. L : Further study of central stimulation from sympathomimetic amines. *J. Pharmacol. & Exper. Therap* 71·62-74 (Jan.) 1941

336 Selye, Hans Compensatory atrophy of the adrenals. *J. A. M.A.* 115·2246-2252 (Dec. 28) 1940

337. Sevringhaus, Aura E · Cytology of pituitary gland In *Association for Research in Nervous and Mental Diseases:* The

pituitary gland. Baltimore, Williams & Wilkins Company, 1938, vol 17, pp 69-117

8 Sevringhaus, E. L.. Diagnostic and therapeutic problems of obesity *J. Michigan M Soc.* 42 530-536 (July) 1943

39 Sevringhaus, E. L *Endocrine therapy in general practice Ed. 5.* Chicago, The Year Book Publishers, Inc, 1945, 253 pp

340. Seward, B. P A clinical study of the mild grades of hypothyroidism *Ann. Int Med.* 9 178-188 (Aug) 1935

341 Sheehan, H L Simmonds' disease due to post-partum necrosis of the anterior pituitary *Quart J Med n s* 8 277-309 (Oct) 1939

342 Shepardson, H C Insulin fattening in ambulatory patient *California & West Med* 40 14-18 (Jan) 1934

343 Short, J J Increasing weight with insulin, preliminary report *J Lab & Clin Med* 14 330-335 (Jan) 1929

344 Short, J J · Extreme obesity followed by therapeutic reduction of two hundred and thirty-nine pounds *J A M A* 111·2196-2197 (Dec 10) 1938

345 Short, J J Increase of electrocardiographic changes with obesity *Proc Life Ext. Exam* 1 82-85 (July-Aug) 1939

346 Short, J J The effect of increasing age on the blood pressures of 9,926 individuals according to sex and weight groups *Proc Life Ext Exam* 2 35-40 (Mar -Apr) 1940

347 Short, J J Obesity In Bridges, M A *Dietetics for the clinician Ed.* 4, Philadelphia, Lea & Febiger, 1941, p 463

348. Short, J J, and Currence, J DeP · An attempt to mobilize lipoids from storage depots by deep massage and increased tissue temperatures *J Lab & Clin Med* 24 395-397 (Jan) 1939

349 Short, J J, and Johnson, H J The increased metabolism of obesity, use and abuse of metabolic stimulants *J A M A* 106 1776-1779 (May 23) 1936

350 Short, J J, and Johnson, H J The effect of overweight on vital capacity *Proc Life Ext Exam* 1 36-41 (Mar -Apr) 1939

351. Short, J J, and Johnson, H J An evaluation of the influenc of overweight on blood pressures of healthy men, a stud of 3516 individuals applying for periodic health examin tions *Am. J M Sc* 198 220-224 (Aug) 1939

H J Use of benzedrine sulfate by psychopat

the problem of addiction. *Brit. M. J.* 2:285-286 (Sept. 1) 1945

353. Silver, Solomon: A new danger in dinitrophenol therapy; agranulocytosis with fatal outcome *J.A.M.A.* 103:1058 (Oct. 6) 1934

354. Silver, Solomon, and Bauer, Julius: Obesity, constitutional or endocrine? *Am. J. M. Sc.* 181:769-777 (June) 1931.

355. Simkins, Samuel: Dinitrophenol and desiccated thyroid in the treatment of obesity; a comprehensive clinical and laboratory study. *J.A.M.A.* 108:2110-2117 (June 19); 2193-2199 (June 26) 1937.

356 Simmonds, M.: Ueber Hypophysisschwund mit tödlichem Ausgang *Deutsche med. Wchnschr.* 40.322-323 (Feb. 12) 1914

357. Simons, A · Crampi bei amyotrophischer Lateralsklerose. Mit einem Anhang: Untersuchung der Aktionsströme der Muskeln während des Crampus *Ztschr. f. d. ges. Neurol. u. Psychiat.* 15:23-28, 1911; 19:377-397, 1913

358. Smith, A. E.: Use of amphetamine sulfate in control of obesity *J.A.M.A.* 123:1117 (Dec. 25) 1943

359. Smith, Austin: Drugs for obesity. *J.A.M.A* 134:527-529 (June 7) 1947.

360. Smith, H. L., and Willius, F. A.: Adiposity of the heart; a clinical and pathologic study of one hundred and thirty-six obese patients. *Arch. Int Med.* 52.911-931 (Dec.) 1933

361. Smith, P. E. The disabilities caused by hypophysectomy and their repair; the tuberal (hypothalamic) syndrome in the rat *J.A.M.A.* 88:158-161 (Jan. 15) 1927.

362. Smith, P. E.: Hypophysectomy and a replacement therapy in the rat *Am. J. Anat.* 45:205-256 (Mar.) 1930.

363 [illegible] Obesity, [illegible] d retinal [illegible] *Quart. J. Med.* 8:51-68 (Jan.) 1939.

364 Soskin, Samuel, and Levine, R.: Recent advances in physiology of the thyroid and their clinical application *Arch. Int Med.* 74:375-383 (Nov.) 1944.

365. Spriggs, Edmund: Discussion on the causes of and treatment of obesity. *Proc. Roy Soc. Med.* 29:411-430 (Nov. 26) 1935.

BIBLIOGRAPHY

366 Starr, H. F.: Effect of excessive abdominal girth on mortality. *South M. & S J* 105 456 (Oct.) 1943

367. Stewart, R M: Localized cranial hyperostosis in the insane *J. Neurol. & Psychopath* 8 321-331 (Apr) 1928

368 Stiefler, Georg. Über hypophysär Fettsuchtals Restzustand eines Falles von Encephalitis lethargica *Monatschr f Psychiat. u Neurol* 50·123-126, 1921

369. Strang, J. M, and Evans, F A The energy exchange in obesity *J. Clin Investigation* 6 277-289 (Oct) 1929

370 Strang, J. M, McClugage, H B, and Evans, F. A Further studies in the dietary correction of obesity *Am J M Sc* 179 687-694 (May) 1930

371 Strang, J M, McClugage, H B, and Evans, F A The nitrogen balance during dietary correction of obesity *Am J M Sc* 181 336-349 (Mar) 1931.

372 Strouse, S, and Dye, M Studies on metabolism of obesity, relation between food intake and body weight in some obese persons *Arch Int Med* 34 267-274 (Sept) 1924

373. Strouse, Solomon, Wang, C C, and Dye, Marie Studies on the metabolism of obesity, preliminary report *J A M A* 82 2111-2112 (June 28) 1924

374 Strouse, Solomon, Wang, C C, and Dye, Marie Studies on the metabolism of obesity II Basal metabolism *Arch Int Med* 34 275-281 (Sept) 1924

375 Swanson, E E, Scott, C C, Lee, H M, and Chen, K. K Comparison of the pressor action of some optical isomers of sympathomimetic amines *J Pharmacol & Exper Therap* 79 329-333 (Dec) 1943

376 Tainter, M. L Actions of benzedrine and propadrine in the control of obesity *J Nutrition* 27 89-105 (Jan) 1944.

377. Tainter, M. L, Stockton, A B, and Cutting, W C Dinitrophenol in the treatment of obesity *J A M A* 105 332-336 (Aug 3) 1935

378 Talbot, N B Obesity in children *M Clin North America* 29 1217-1230 (Sept) 1945

379. Talbot, N B, Wilson, E B, and Worcester, Jane. Basal metabolism of girls, physiologic background and application of standards *Am J Dis Child* 53 273-347 (Jan) 1937

380 Tannenbaum, Albert Relationship of body weight to cancer incidence *Arch Path.* 30 509-517 (Aug.) 1940

381. Tepperman, Jay, Brobeck, J. R, and Long, C N H: The effects of hypothalamic hyperphagia and of alterations in feeding habits on the metabolism of the albino rat. *Yale J. Biol & Med.* 15:855-874 (July) 1943.

382. Terry, A H. Obesity and hypertension *J A.M.A.* 81:1283-1284 (Oct 13) 1923

383 Thompson, W O · Obesity in children. *Proc. Inter-State Postgrad. M A. North America.* (1943) pp 96-100, 1944

384 Thorn, G W, Quinby, J T., and Clinton, M, Jr: Comparison of the metabolic effects of isocaloric meals of varying composition, with special reference to prevention of postprandial hypoglycemic symptoms. *Ann. Int. Med.* 18· 913-919 (June) 1943.

385 Tuerkischer, E, and Wertheimer, E.: Glycogen and adipose tissue *J Physiol.* 100:385-409 (Mar) 1942

386 Tunbridge, R E: The treatment of obesity. *Clin J.* 67 154-162 (Apr) 1938

387 Von Noorden, Carl, *Metabolism and practical medicine.* Chicago, W T Keener & Company, 1907, vol 1, 452 pp, vol. 2, 525 pp, vol. 3, 1320 pp

388 Waldorp, C P: An original clinical interpretation of Dercum's disease (adiposis dolorosa). *Endocrinology.* 8:54-60 (Jan) 1924

389. Waller, J. V, Kaufman, M R, and Deutsch, Felix Anorexia nervosa a psychosomatic entity. *Psychosom. Med.* 2.3-16 (Jan) 1940

390. Walsh, T G Postencephalitic obesity; report of cases *J A.M.A* 87·305-307 (July 31) 1926

·391. Wang, C C, Strouse, Solomon, and Morton, Zelma O: The metabolism of obesity. V. Mechanical efficiency. *Arch. Int Med* 45 727-733 (May) 1930.

392. Wang, C C, Strouse, Solomon, and Saunders, Alice D. Studies on the metabolism of obesity. III The specific dynamic action of food *Arch Int Med* 34:573-583 (Oct) 1924

393. Wang, C C, Strouse, Solomon, and Saunders, Alice D: The metabolism of obesity. IV. The distribution of energy production after food *Arch. Int. Med.* 36·397-417 (Sept) 1925.

394 Ward, J A Obesity and its management *South M J* 31 1280-1286 (Dec) 1938

395 Warkany, Josef, Frauenberger, G S, and Mitchell, A G

Heredofamilial deviations I The Laurence-Moon-Biedl syndrome *Am. J. Dis Child.* 53 455-470 (Feb) 1937

396. Watts, J. W . The influence of the cerebral cortex on gastro-intestinal movements *J A M A* 104 355-357 (Feb 2) 1935

397. Weisman, A I , and Reifer, Paul Simple method of determining correct thyroid dosage in cases of thyropituitary disease *M. Rec* 142 421-422 (Nov 6) 1935

398 Weiss, E : Neurocirculatory asthenia, need for psychosomatic approach and revised terminology *Psychosom Med* 5 93-96 (Jan) 1943

399 Wells, H G Adipose tissue, a neglected subject *J A M A* 114 2177-2183 (June 1) 1940

400. Werner, A A , and Weir, D. C Obesity in the adult *J Missouri M A* 35 385 388 (Oct) 1938

401 Werthessen, Nicholas The significance of subnormal respiratory quotient values induced by controlled feeding in the rat *Am J Physiol* 120 458-465 (Nov) 1937

402. Wetzel, N C. Physical fitness in terms of physique, development and basal metabolism with a guide to individual progress from infancy to maturity, a new method for evaluation *J A M A* 116 1187-1195 (Mar 22) 1941

403 Wheatley, M D The hypothalamus and affective behavior in cats, a study of the effects of experimental lesions, with anatomic correlations *Arch Neurol & Psychiat* 52 296-316 (Oct) 1944

404. Whipple, A O Present day surgery of the pancreas *New England J Med* 226 515-526 (Mar 26) 1942

405. White, P D *Heart disease Ed 3*, New York, The Macmillan Company, 1944, 1025 pp

406. Winkelman, M W , and Eckel, J L Adiposis dolorosa (Dercum's disease) , a clinicopathologic study *J A M A* 85 1935-1939 (Dec 19) 1925

407. Wilder, R. M The management of obesity *J Am Dietet A* 6.91-100 (Sept) 1930

408 Wilder, R. M The regulation of the weight of the body *Internat. Clin* 1 30-41 (Mar) 1932

409 Wilder, R. M : The treatment of obesity *Internat Clin* 4 1-21 (Dec) 1933

410 Wilder, R M , and Wilbur, D L Diseases of metabolism and nutrition, review of certain recent contributions *Arch Int Med* 61·297-365 (Feb) 1938

411. Wilder, R. M., Smith, Florence H., and Sandiford, Irene. Observations on obesity. *Ann. Int. Med.* 6:724-742 (Dec.) 1932.
412. Wilens, S L.. Bearing of general nutritional state on atherosclerosis *Arch. Int. Med.* 79:129-147 (Feb.) 1947.
413 Wiley, F H., and Newburgh, L. H.: The doubtful nature of "Luxuskonsumption." *J. Clin. Investigation.* 10·733-744 (Oct) 1931.
414. Wilhelmj, C. M.: Specific dynamic action of food *Physiol. Rev.* 15:202-220 (Apr.) 1935.
415. Willius, F. A.: Discussion. *J.A M.A.* 101:424 (Aug. 5) 1933.
416. Willson, D. M, Power, M. H., and Kepler, E. J.: Alkalosis and low plasma potassium in a case of Cushing's syndrome; a metabolic study. *J. Clin. Investigation.* 19.701-707 (Sept) 1940.
417. Winkler, A. W., Tavietes, P. H, Robbins, C. L., and Man, E B.: Tolerance to oral thyroid and reaction to intravenous thyroxine in subjects without myxedema *J. Clin. Investigation.* 22:535-544 (July) 1943.
418. Wood, J. E, and Cash, J. R: Obesity and hypertension: clinical and experimental observations. *Ann. Int. Med* 13·81-90 (July) 1939
419 Yorke-Davies, N. E: Thyroid tabloids in obesity. *Brit. M. J.* 2 42-43 (July 7) 1894.
420. Ziegler, L. H.: Lipodystrophies Report of seven cases. *Brain* 51·147-167 (June) 1928.
421. Zondek, Hermann. *The diseases of the endocrine glands. Ed 4.* (Translated by Carl Prausnitz Giles) Baltimore, The Williams & Wilkins Company, 1944, 496 pp.
422. Zondek, Herman: Obesity. *J.A.M A.* 134:1197 (Aug. 2) 1947.

THIS BOOK

Obesity...

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was set, printed, and bound by the Pantagraph Printing and Stationery Company of Bloomington, Illinois. The type face is Intertype Garamond, set 12 point on 13 point The type page is 23 x 41 picas. The text paper is 70 lb. White Wove Warren's Olde Style The cover is Fabrikoid 7055, grain M-3, plia Med., Finish B



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